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EFFECTS OF CORTISONE ACETATE ON RHEUMATOID ARTHRITIS

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A crystalline steroid was isolated from the adrenal cortex by Kendall and co-workers in 1935.[1] Its chemical formula, 17-hydroxy-11-dehydrocorticosterone, was determined by them in 1938.[2] Prior to 1948 so little of the hormone, known as Kendall's compound E, was available for research that only a few facts regarding its physiologic activity were established. Its use in rats subjected to adrenalectomy improved muscle activity, as measured by the muscle-work test [3] and increased physiologic resistance to stress, cold and certain toxic substances.[4] In young rats growth was retarded and weight loss was induced.[5] A definite influence on carbohydrate metabolism was established: administration to partially depancreatized rats intensified the diabetic state [6]; administration to normal rats produced transient hyperglycemia and glycosuria.[7] In 3 human subjects with coexisting Addison's disease and diabetes mellitus, the diabetes was augmented when compound E was given in daily doses of 8 to 20 mg.[8]

It was not until 1946, after more than two years of intensive research had been completed in cooperation with Kendall and his staff at the Mayo Clinic, that compound E, now known as cortisone, was finally synthesized by Sarett in the Merck research laboratories from a bile acid (desoxycholic acid). Continued cooperation between Kendall and Merck scientists resulted in improvements in the synthesis, but not until late in 1948 had sufficient material accumulated to provide the small amounts of compound E necessary for preliminary clinical evaluations. More recently compound E has been made and used in the form of the acetate (cortisone acetate). The product is still extremely scarce, but its physiologic activities are now being investigated at several research centers.

Application of the Drug to Rheumatoid Arthritis.—The clinical course of rheumatoid arthritis is not always one of relentless progression. The disease is capable of spontaneous reversibility, and not infrequently the course is interrupted by periods of partial or complete remission; complete remissions may last for months or years, and spontaneous permanent inactivations are not rare. Moreover, certain procedures, such as injections of typhoid vaccine, starvation or a surgical operation, may sometimes induce temporary amelioration. Two conditions, pregnancy [9] and jaundice from biliary obstruction or hepatitis,[10] are potent antagonists of rheumatoid arthritis. Neither state is known to influence favorably the course of proved bacterial infection, yet the intercurrence of pregnancy or jaundice in patients with rheumatoid arthritis produces temporary remission, partial or complete, in a high percentage of instances. Because these facts do not harmonize with the unproved bacterial theory of the causation of rheumatoid arthritis, Hench [11] speculated that some biochemical disturbance might be at fault in the pathogenesis. He conjectured that a bisexual hormone, possibly an adrenocortical hormone, might be involved in the curious antirheumatic effect of pregnancy, jaundice and other states. In September 1948 Hench, Kendall, Slocumb and Polley [11b] administered compound E to a patient with severe rheumatoid arthritis; rapid and striking improvement in the clinical manifestations of the disease resulted.

Observations of Hench, Kendall, Slocumb and Polley.—These investigators recently reported the effects of compound E or its acetate on 14 patients with severe, or moderately severe, rheumatoid arthritis. The duration of the disease was from four and one-half months to five years, and the erythrocyte sedimentation rates ranged from 108 to 62 mm. in one hour (Westergren method). Prompt and striking improvement in the musculoskeletal, constitutional and laboratory manifestations of the disease resulted in each case. Within a

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1. (*a*) Mason, H. L.; Myers, C. S., and Kendall, E. C.: The Chemistry of Crystalline Substances Isolated from the Suprarenal Gland, J. Biol. Chem. **114**: 613-631 (July) 1936; (*b*) Kendall, E. C.: Some Observations on the Hormone of the Adrenal Cortex Designated Compound E, Proc. Staff Meet., Mayo Clin. **24**:298-301 (May 25) 1949.

2. Mason, H. L.; Hoehn, W. M., and Kendall, E. C.: Chemical Studies of the Suprarenal Cortex; IV. Kendall.[1b] Structures of Compounds C, D, E, F and G, J. Biol Chem. **124**: 459-474 (July) 1938.

3. Ingle, D. J., and Kendall, E. C.: Influence of Amorphous Fraction from Adrenal Cortex on Efficiency of Muscle, Proc. Soc. Exper. Biol. & Med. **45**: 602-606 (Nov.) 1940. Ingle, D. J., and Kuizenga, M. H.: The Relative Potency of Some Adrenal Cortical Steroids in the Muscle-Work Test, Endocrinology **36**: 218-225, 1945.

4. Kendall, E. C.: The Adrenal Cortex, Arch. Path. **32**: 474-501 (Sept.) 1941.

5. Wells, B. B., and Kendall, E. C.: The Influence of Corticosterone and C 17 Hydroxydehydrocorticosterone (Compound E) on Somatic Growth, Proc. Staff Meet., Mayo Clin. **15**: 324-328 (May 22) 1940.

6. Ingle, D. J., and Thorn, G. W.: A Comparison of the Effects of 11-Desoxycorticosterone Acetate and 17-Hydroxy-11-Dehydro-Corticosterone in Partially Depancreatized Rats, Am. J. Physiol. **132**: 670-678, 1941. Ingle, D. J.: Diabetrogenic Effect of Some Cortin-Like Compounds, Proc. Soc. Exper. Biol. & Med. **44**: 176-177, 1940. Kendall.[4]

7. Ingle, D. J.: The Production of Glycosuria in the Normal Rat by Means of 17-Hydroxy-11-Dehydrocorticosterone, Endocrinology **29**: 649-652 (Oct.) 1941.

8. Sprague, R. G.; Gastineau, C. F.; Mason, H. L., and Power, M. H.: Effects of Synthetic 11-Dehydrocorticosterone (Compound A) in a Subject with Addison's Disease, Am. J. Med. **4**: 175-185 (Feb.) 1948.

9. Hench, P. S.: The Analgesic Effect of Hepatitis and Jaundice in Chronic Arthritis, Fibrositis and Sciatic Pain, Ann. Int. Med. **7**:1278-1294 (April) 1934.

10. Hench, P. S.: The Ameliorating of Pregnancy on Chronic Atrophic (Infectious, Rheumatoid) Arthritis, Fibrositis and Intermittent Hydrarthrosis, Proc. Staff. Meet., Mayo Clin. **13**: 161-167 (March 16) 1938.

11. (*a*) Hench, P. S.: The Potential Reversibility of Rheumatoid Arthritis, Proc. Staff Meet., Mayo Clin. **24**:167-178 (March 30) 1949. (*b*) Hench, P. S.; Kendall, E. C.; Slocumb, C. H., and Polley, H. F.: The Effect of a Hormone of the Adrenal Cortex (17-Hydroxy-11-Dehydrocorticosterone: Compound E) and of Pituitary Adrenocorticotropic Hormone on Rheumatoid Arthritis: Preliminary Report, ibid. **24**: 181-197 (April 13) 1949.

few days there was decided lessening of the muscular and articular stiffness, with less articular aching, tenderness and pain on motion, and significant improvement in function of muscles and joints. The favorable effects often began within a few hours after the first injection of cortisone and were pronounced within a few days. Articular swellings usually diminished, fairly rapidly and completely in some cases but tardily and incompletely in others. Constitutional symptoms subsided rapidly, often with increase in appetite, corresponding gain in weight and strength, loss of "toxic" feeling and the development of a strong sense of well-being.

In 9 of the 14 patients compound E or its acetate was given for short periods ranging from eight to sixty-one days. In 8 of these 9 patients the symptoms and signs began to return within two to four days after the discontinuance of endocrine therapy; the return progressed slowly in 6 but rapidly in 2. One patient retained most of the improvement five months after cessation of treatment with the preparation.[12] Five of the 14 patients received the compound either continuously or intermittently for prolonged periods of two to four months. During administration of the drug they were almost, but not entirely, free of symptoms, but during periods when its administration was interrupted exacerbations of the disease promptly ensued. Prolonged administration of cortisone in 1 patient produced signs of an endocrine disturbance characterized by mild acne and hirsutism, rounding of the facial contour, amenorrhea and mental depression; these were reversible features which disappeared when the administration of cortisone was discontinued.[12]

In each of the 14 cases the erythrocyte sedimentation rate diminished notably, the fall in rate beginning usually within three to nine days after the first administration of compound E. Except in 3 cases, the rates returned to normal within ten to thirty-five days. Other corrective influences in initially abnormal laboratory determinations were noted also: increased serum globulin levels and lowered albumin-globulin ratios, when present, tended to become normal within a few days; urinary excretions of 17-ketosteroids were reduced and excretions of corticosteroids were increased; erythrocyte counts and hemoglobin values improved; the synovial membranes, examined in 1 case before and after the use of cortisone, showed histologic evidence of healing.

Our Investigation.—The effects of administration of cortisone were observed by us in 8 patients with rheumatoid arthritis.[13] The patients were studied in two groups: (*a*) 5 patients with severe and decidedly active disease, and (*b*) 3 patients with less severe rheumatoid arthritis (2 with moderate and 1 with mild disease). For the sake of simplicity of presentation, the two groups will be discussed separately.

EFFECTS OF CORTISONE IN SEVERE RHEUMATOID ARTHRITIS

Each of the 5 patients with severe rheumatoid arthritis had involvement of multiple peripheral joints and great disability; 2 had involvement of the spine also. The duration of the disease varied from four to fifteen years. Erythrocyte sedimentation rates before the use of cortisone were (in order of cases): 74, 128, 70, 97 and 80 mm. in one hour (Westergren method).

Cortisone acetate was administered to each patient for eight days. In regard to the daily dose we were guided by the experience of Hench, Kendall, Slocumb and Polley. Four of the 5 patients received an initial dose of 300 mg. given intramuscularly on the first day and 100 mg. daily thereafter for seven days. One patient (case 3) received 200 mg. on the first and second days and 100 mg. daily thereafter for six days; this patient had coexisting diabetes mellitus, and it was considered inadvisable to risk an initial dose of 300 mg.

Controls.—To provide adequate controls, daily intramuscular injections of a control substance consisting of a fine suspension of cholesterol, identical in appearance to the suspension of cortisone, were given for two days prior to and five days after actual administration of cortisone. Improvement started after the administration of cortisone and regression set in after withdrawal of the agent; the control substances, given without the patients' knowledge, did not influence the course of disease. Analgesics and other medicaments were withheld during the periods when cortisone and the control substance were given.

REPORT OF CASES

CASE 1.—*History and Course Prior to Administration of Cortisone.*—M. L., a man aged 53, had severe rheumatoid arthritis of ten years' duration involving multiple peripheral joints. The first musculoskeletal symptoms dated to 1939, and for the first three years the articular manifestations were episodic in type. From 1942 to 1947 the disease was chronic and progressive, with extension to involve an increasing number of joints. In the fall of 1947 gold salt therapy was begun, and by March 1948 the disease was in almost complete clinical remission. Because of gold dermatitis, chrysotherapy was discontinued in October 1948. In December 1948 severe exacerbation of the arthritis occurred, and during the next six months the disability of the patient became progressively greater. He lost more than 20 pounds (9.1 Kg.) in body weight, experienced pronounced fatigue and became emotionally unstable and mentally depressed. Finally pain and disability were so severe that he resorted to frequent doses of codeine (as much as 3 or 4 grains [0.19 or 0.26 Gm.] in a day) in addition to large daily amounts of salicylates.

His functional capacity was greatly restricted. Because of disability in the fingers, wrists, elbows and shoulders he was unable to shave or comb his hair in the morning; these acts were postponed until about 2 o'clock in the afternoon, by which time he had limbered up somewhat. To dress himself in the morning was an exhausting and painful procedure, and at times it took him fifteen to twenty minutes to lace his shoes. He was able to get out of a chair by himself, but only with great effort; sometimes this took as long as ten minutes. He had much difficulty in feeding himself, especially in the morning, and it was hard for him to wring out a wash cloth, even partially.

Examination of the peripheral joints prior to the administration of cortisone revealed moderate to severe tenderness, swelling, limitation of motion and pain on forced motion of the proximal interphalangeal and metacarpophalangeal joints of both hands, both wrists and both elbows. Interosseous atrophy of the muscles of the hands was moderate in degree. The metatarsophalangeal joints of both feet were decidedly swollen and tender. The right ankle was severely swollen, tender and painful on motion; similar but less pronounced conditions were present in the left ankle. The right hip and both shoulders were moderately restricted on motion and painful on attempted forced motion. There was a rheumatoid nodule measuring 1.5 by 1.5 cm. on the dorsum of the right tarsal region, and bilateral olecranon bursitis was present. The erythrocyte sedimentation rate was 74 mm. in one hour.

12. Hench, P. S.: Personal communication to the authors.
13. One of us (Dr. Boland) was among the five physicians invited to the Mayo Clinic in March 1949 to observe the effects of cortisone. Thereafter a small quantity of the preparation was made available to us by Merck & Co., Inc., Dr. James Carlisle, medical director.

Course with Administration of Cortisone.—After we began to give cortisone improvement was rapid: within ten hours, rest pain and stiffness were greatly reduced. Whereas the patient had previously given himself frequent injections of codeine, he found no need even for acetylsalicylic acid. By the next morning he had acquired a sense of well-being and strength; his appetite for breakfast was excellent, and for the first time in several months even the "cool and almost hard-boiled egg tasted fine." He was able to wash, shave, comb his hair and dress himself by 7 o'clock. Within forty-eight hours there was a significant reduction in joint swelling and an increase in motion; joint tenderness was decreased 75 per cent. By the fourth day rest pain had disappeared entirely; only 10 per cent of the original stiffness remained, and there was only slight swelling in a few joints. Swelling of the olecranon bursae disappeared almost entirely, and the rheumatoid nodule diminished to one-half its original size. Euphoria was appreciable, and a psychiatric consultant judged the patient as "almost hypomanic"; he made intelligent and purposeful business deals by telephone, talked rapidly with gesticulations, voluntarily exhibited his calisthenic prowess to visitors and generally "felt great." Improvement was sustained throughout the period of cortisone administration; the over-all clinical improvement was estimated at 85 per cent. The erythrocyte sedimentation rate decreased to 49 mm. in 1 hour.

Course Following Withdrawal of Cortisone.—An acute flare-up of pain and swelling of the first and second metacarpophalangeal joints of the right hand developed thirty-six hours after the last injection of cortisone. In forty-eight hours limitation of motion, pain, stiffness, tenderness and swelling began to recur in all the involved joints. By the seventh day the patient was again mentally depressed; objectively, the joints were as bad as, or worse than, they had been before the administration of cortisone. During the succeeding month he lost 10 pounds (4.5 Kg.) in body weight and became despondent; the sedimentation rate rose to 77 mm. in one hour, and disability progressed. He was "more crippled than at any time during the past twenty years."

CASE 2.—*History and Course Prior to Administration of Cortisone.*—J. S., a woman aged 56, was extremely disabled from rheumatoid arthritis of four years' duration. For the first three years the disease was mild and articular involvement was confined to the metatarsophalangeal joints. In the spring of 1948 the process became more active and began to spread gradually to other joints. In December 1948, five months prior to the administration of cortisone, the disease became severe; within a few weeks practically all the peripheral joints, except the terminal interphalangeal joints of the fingers and toes, were involved. During this five month period she lost 35 pounds (15.9 Kg.) in weight, had a daily fever (100.6 to 102 F.), demonstrated pronounced anorexia, fatigue and weakness, and became greatly discouraged and mentally depressed. Joint pain was pronounced, and she reacted to attempted movement of her joints with fear, resistance and resentment. In addition to large doses of salicylates, she required several injections of codeine each day to control pain.

Examination of the joints revealed bilateral involvement of the shoulders, elbows, wrists, ankles, knees, metacarpophalangeal and metatarsophalangeal joints, sternoclavicular joints and the proximal interphalangeal joints of both hands and feet. These articulations were moderately to severely swollen, painful, tender and limited on motion. The temporomandibular joints were moderately tender, restricted in motion and painful. The erythrocyte sedimentation rate was 128 mm. in one hour (Westergren method), and the erythrocyte count was 3,040,000 cells per cubic millimeter, with 7 Gm. of hemoglobin.

Prior to the administration of cortisone disability was extreme and the patient was confined to bed. Without assistance from an attendant she was unable to sit up in bed, turn on her side, get on and off a bed pan or move her feet over the side of the bed. Because of painful and limited motion of the joints of the arms she was unable to feed herself, comb her hair, brush her teeth, bathe or dry herself, wring out a wash cloth or write. With considerable aid from an attendant she could walk with a painful, cautious, shuffling gait to the bathroom; however, she had to be lifted on and off the toilet seat.

Course with Administration of Cortisone.—Striking mental and physical improvement occurred within twenty-four hours after the patient received the initial injection of 300 mg. of cortisone. Her mental attitude changed and she became alert, cheerful and hopeful. Joint pain and stiffness were greatly lessened, and analgesics were no longer needed. Movement increased remarkably, and she was able to get on and off the bed pan, to aid herself in eating, and to walk to the bathroom without help and with little discomfort. Subjective and objective improvement continued at a rapid pace during the eight days of administration of cortisone. Each day there was further lessening of pain, tenderness and swelling, and movement of the joints increased greatly. On the fifth day she could get in and out of bed unassisted, put on her own slippers and robe, sit down and rise from chairs with ease, turn doorknobs, comb her hair, feed herself and accomplish numerous other acts which formerly were impossible. Despite advanced quadriceps atrophy, the strength in her legs returned quickly and she was able to walk through the hospital halls with security and confidence. At the end of eight days she estimated that approximately 90 per cent of her stiffness and pain had disappeared, and joint swellings were reduced notably. The erythrocyte sedimentation rate was reduced from 128 to 53 mm. in one hour, and the erythrocyte count increased 930,000 cells per cubic millimeter. Her temperature had remained normal since the second day of administration of cortisone. Her appetite was ravenous, and she sustained a total weight gain of 8¼ pounds (4 Kg.), an average of 1 pound (0.5 Kg.) a day.

Course After Withdrawal of Cortisone.—Improvement was maintained for approximately forty-eight hours after the use of cortisone was discontinued; then a recrudescence of symptoms ensued. For the next five days increased pain, tenderness, stiffness and swelling of the joints occurred, much of the gain in functional capacity was lost and daily fever (99.2 to 101 F.) returned. However, the manifestations then began to subside again, and improvement thereafter was progressive. Whereas originally she was completely bedridden and febrile, with the erythrocyte sedimentation rate 128 mm. in one hour, two months after cessation of administration of cortisone she was ambulatory and afebrile, with the erythrocyte sedimentation rate 44 mm. in one hour; approximately 75 per cent of the maximal improvement was regained.

CASE 3.—*History and Course Prior to Cortisone Therapy.*—L. D., a man aged 71, had severe rheumatoid arthritis involving multiple peripheral joints and the entire spine. In 1944, while he was under great emotional stress, the disease began acutely; within four weeks the wrists, elbows, shoulders, ankles, knees and small joints of the hands and feet were involved. Disability in these joints persisted; pain, aching, stiffness and limitation of motion of the spine intervened, with gradual spread to higher levels. Various types of therapy were tried, but response was indifferent to each; treatment with gold salts was given for one year in 1947 without noteworthy effect.

Examination of the musculoskeletal system prior to the administration of cortisone revealed moderate to severe swelling, tenderness and limitation of motion in the shoulders, elbows, wrists, ankles, knees, metacarpophalangeal and metatarsophalangeal joints bilaterally and the proximal interphalangeal articulations of both hands. There was pronounced flexion deformity with ulnar deviation of the fingers of the right hand. Both temporomandibular joints were tender, and motion of the jaw was slightly restricted. There was decided atrophy of various muscle groups, particularly the quadriceps and interosseous muscles. Typical poker-back deformity, with almost complete immobility of the lumbar and dorsal segments and with moderate restriction of cervical motion, was present; the chest expansion equaled 1½ inches (4 cm.). Roentgenographic changes characteristic of rheumatoid spondylitis were present. The erythrocyte sedimentation rate was 70 mm. in one hour.

The patient had had uncomplicated diabetes mellitus for ten years. For several months prior to administration of cortisone the diabetes was controlled adequately by a measured diet and 10 units of protamine zinc insulin daily.

Course with Administration of Cortisone.—Two hundred mg. of cortisone were given for two days and then 100 mg. were

given daily for six subsequent days. Improvement was slow and only moderate in degree. Forty-eight hours after the initial injection, rest pain and stiffness began to recede and general strength improved. Mental depression, which was pronounced beforehand, disappeared. The patient became jovial and witty, but true euphoria did not develop. Joint movement and functional capacity improved moderately within the eight days, but not to the degree noted in the other 4 cases. His appetite was good but not ravenous. Joint tenderness decreased moderately, but appreciable reduction in joint swellings did not occur. Aching and stiffness of the neck and upper part of the back diminished, but the objective observations referable to the spine did not change significantly. The erythrocyte sedimentation rate diminished from 70 to 34 mm. in one hour at the end of the eight day period.

Although the patient was on a measured diabetic diet, glycosuria was noted twenty-four hours after the initial injection of 200 mg. of cortisone. Thereafter 30 to 50 units of insulin were required daily to control the diabetes. Three days after withdrawal of the endocrine substance the insulin requirement of the patient reverted to 10 units daily.

Course After Withdrawal of Cortisone.—Retrogression after the withdrawal of cortisone was slow, and although improvement had not been extensive, the gains which had been made were retained for almost two weeks. At the end of one month the symptoms and observations had increased to their original intensities and the sedimentation rate had returned to 60 mm. in one hour.

CASE 4.—*History and Course Prior to Administration of Cortisone.*—A. H., a man aged 52, had suffered from rheumatoid arthritis for fifteen years. From 1947 to 1948 the clinical course had been punctuated with partial remissions and exacerbations. For more than one year, however, he had been almost totally incapacitated because of severe involvement of multiple peripheral joints and the entire spine. For eight weeks prior to the administration of cortisone he had been unable to dress himself and was bedfast except for bathroom privileges. He was unable to put on his socks or button his pajamas and was barely able to feed himself. Late in the afternoon he managed to shave with an electric razor, but it was impossible for him to comb the back of his hair and both hands were needed to brush his teeth. He took at least fifteen minutes to get out of bed in the morning, and even late in the day he needed assistance in getting on and off a toilet seat. He walked with a painful shuffling gait, and after going approximately 30 feet (9 meters), it was necessary for him to rest before proceeding farther. Constitutional reaction was pronounced, with anorexia, weight loss of 20 pounds (9.1 Kg.) in the preceding year, weakness and easy fatigability.

Examination of the musculoskeletal system before the administration of cortisone revealed severe swelling and moderate tenderness, pain and limitation of motion of the elbows, wrists, knees, ankles, metacarpophalangeal and metatarsophalangeal joints bilaterally and the proximal interphalangeal joints of the fingers. Motion was restricted decidedly in both shoulders and moderately in both hips. The temporomandibular joints were tender, painful on motion and moderately restricted. The right sternoclavicular joint was swollen and tender. Advanced muscle atrophy, particularly of the interosseous, shoulder girdle and quadriceps group of muscles, was present. Examination of the spine revealed typical signs of rheumatoid spondylitis with pronounced restriction of motion of the lumbar, dorsal and cervical segments and limitation of chest expansion to 1 inch (2.5 cm.). Roentgenograms of the spine revealed partial ankylosis of both sacroiliac joints and moderate paraspinal ligamentous calcification in the lower dorsal and upper lumbar regions. The erythrocyte sedimentation rate was 97 mm. in one hour, and the erythrocyte count was 4,040,000 cells per cubic millimeter with 10 Gm. of hemoglobin.

Course with Administration of Cortisone.—Improvement was gradual and progressive. After thirty-six hours, rest pain disappeared almost entirely, and stiffness and mental depression began to subside. After three days joint pain on weight-bearing and motion decreased, and articular function and muscle strength were decidedly improved; he walked a distance of 300 feet (90 meters) and with a longer stride and more rapid pace. By the fourth day 75 per cent of the stiffness had disappeared and the range of motion in the fingers, wrists and elbows was greater. For the first time in several weeks he was able to comb the back of his hair, make a fairly tight fist, scratch his ears, put his socks on and button his pajamas. On the fifth day he awakened with an urge to exercise and accordingly walked up and down the corridor a number of times, visiting various patients en route. He could sit down on, and arise from, chairs with ease and could slowly and cautiously climb a flight of stairs. He had a new zest for living and began to make plans for the future. Appetite was augmented and extra food was requested between meals; a weight gain of 12½ pounds (5.7 Kg.) was recorded during the eight day period of cortisone administration. Back and neck discomfort disappeared almost entirely, cervical motion was notably increased and chest expansion increased ½ inch (1.27 cm.). Reductions in joint swellings were definite but not pronounced; in general, articular swellings were reduced about 30 per cent. At the end of eight days the sedimentation rate had fallen from 97 to 56 mm. in one hour.

Course Following Withdrawal of Cortisone.—A gradual return of aching and stiffness began forty-eight hours after cessation of administration of cortisone, and thereafter analgesics were requested. Joint tenderness, swelling and restriction of motion, together with muscle weakness, returned slowly over a period of four weeks. At the end of this period most of the gain in functional capacity had been lost. Two months after withdrawal of the drug the articular manifestations were almost identical to those noted prior to the administration of cortisone, although the patient believed that his energy and mental outlook remained improved.

CASE 5.—*History and Course Prior to Administration of Cortisone.*—M. S., a woman aged 49, had severe peripheral rheumatoid arthritis of eleven years' duration. The disease began insidiously in 1936 and, except for some improvement following gold salt therapy in 1942 and 1943, progression had been steady. For six months prior to the administration of cortisone disability was extreme; pain, weakness and fatigability were intense and joint function had decreased rapidly. The patient could walk for short distances but did so in a stooped position and with an awkward gait, dragging her feet and clutching various objects for support as she went along; agonizing pain accompanied each step. To arise from a sitting position was a laborious feat which she accomplished by rocking from one side to the other. On attempting to sit on a chair or toilet seat she fell heavily and then cried out with pain. With great effort she could slowly get out of bed, moving her legs over the side with her hands and arms. She was unable to lift the bed covers with her hands and maneuvered them with her forearms. Disability of fingers prevented her from turning a radio dial, cutting meat or buttoning clothes; toothpaste was squeezed from the tube by pressure with the forearm. It was impossible for her to brush her hair or teeth or to wash herself until late afternoon. Despite great incapacity and appreciable activity of the disease, she was only mildly depressed mentally, had a fairly good appetite and had not lost weight.

Examination of the musculoskeletal system revealed moderate to severe swelling, tenderness and limitation of motion of the wrists, elbows, shoulders, ankles, knees, metacarpophalangeal and metatarsophalangeal joints bilaterally and the proximal interphalangeal joints of the fingers. The left temporomandibular joint was tender and painful on forced motion, and the left sternoclavicular joint was moderately swollen. Flexion deformity was present in both knees, 15 degrees on the left and 20 degrees on the right. There was decided atrophy of the shoulder girdle and quadriceps muscles and moderate atrophy of the interosseous muscles of the hands. The erythrocyte sedimentation rate was 80 mm. in one hour and the erythrocyte count was 4,140,000 cells per cubic millimeter with 11 Gm. of hemoglobin.

Course with Administration of Cortisone.—Improvement with the use of cortisone was rapid and dramatic. Six hours after the patient received the initial injection of 300 mg. of cortisone, a visitor with whom she was playing cards remarked how much better she was holding and handling the cards. With surprise she found that her fingers moved freely and relatively painlessly, that she could turn the radio dial and pull the bed covers up

with her hands. That evening she swung her legs over the side of the bed, put on her slippers without aid, stood almost straight and gingerly walked about the room with only slight discomfort in the knees. She was able to turn doorknobs with her hands and arise from a chair with little difficulty. She could easily accomplish many acts which were exceedingly difficult a few hours previously. Progress continued, and twenty-four hours after the initial injection of the drug she estimated that

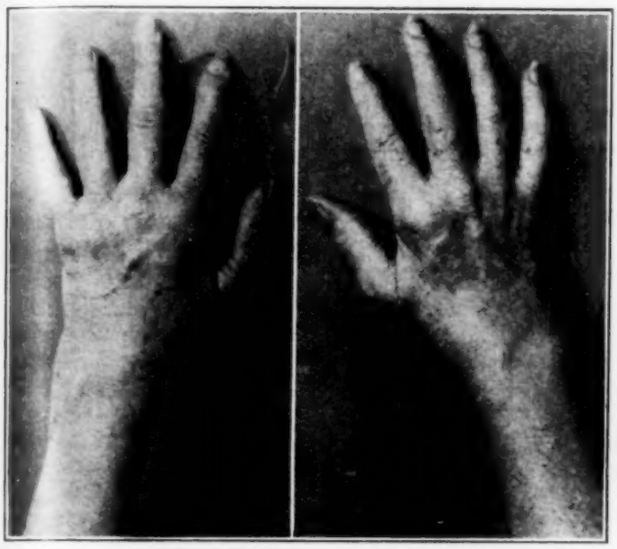

Fig. 1. (case 5).—Appearance of patient's hands before the administration of cortisone; note swellings of the wrists, metacarpophalangeal and proximal interphalangeal joints.

75 per cent of rest pain and stiffness were gone. She was able to brush her hair, wash the back of her neck, squeeze the toothpaste tube with her fingers, pick up fine objects from the floor and dress herself. Euphoria was pronounced, and she chatted almost incessantly about her achievements, gesticulating freely as she talked. Weakness and fatigue lessened remarkably and mild insomnia developed. Swelling, tenderness and range of motion in the joints improved notably by the fourth day; tenderness and swelling of the joints were reduced approximately 50 per cent (figs. 1 and 2). Flexion deformities of the knees decreased from 15 to 5 degrees on the left, and from 20 to 10 degrees on the right. Improvement continued throughout the course of administration, with daily gains in functional accomplishments. Appetite was improved, and a weight gain averaging ¼ pound (0.11 Kg.) a day was recorded. The erythrocyte sedimentation rate decreased from 80 to 59 mm. in one hour (Westergren method), and the erythrocyte count increased 500,000 cells per cubic millimeter during the eight day period.

Course Following Withdrawal of Cortisone.—Improvement was maintained until two days after the withdrawal of cortisone, when pain, stiffness, tenderness and limitation of motion began to return. Regression was gradual over a period of approximately one month, at the end of which time the objective and subjective manifestations had returned almost to their original states and the erythrocyte sedimentation rate had increased to 77 mm. in one hour.

SUMMARY OF CLINICAL EFFECTS OF CORTISONE IN SEVERE RHEUMATOID ARTHRITIS

The immediate result from short term administration of large doses of cortisone in the 5 cases of severe rheumatoid arthritis was decidedly pronounced improvement in 3, pronounced improvement in 1 and moderate improvement in 1 (table).

Effects on the Musculoskeletal System.—The musculoskeletal symptoms began to subside rapidly with the administration of cortisone. In 3 cases the improvement was striking, beginning within six hours after the initial injection in 1 case and within twenty-four hours in 2. Improvement proceeded more slowly and less spectacularly in the remaining 2 cases. One patient, who had been barely able to get out of bed without assistance at 11 o'clock in the morning, when the first injection was given, was able to get in and out of bed with ease and to walk freely about the room in the evening of the same day. Another, who had been unable to bring her hands to her mouth or to handle eating implements, was able to feed herself twenty-four hours after the initial injection.

The first symptoms to subside were muscular and articular stiffness and rest pain. Within twenty-four to forty-eight hours the patients had no further desire for acetylsalicylic acid or other analgesics. Next in order of improvement were lessening of joint pain on motion, increased motion and decreased tenderness of the joints. Reductions in articular swellings were slower in appearing. Although swellings and effusions were reduced greatly in 3 cases, they did not recede entirely during the eight day period of administration of cortisone. A rapid return of muscle strength and joint function, despite advanced muscle atrophy and previously restricted joint motion, was remarkable. Four of the 5 patients had pronounced quadriceps atrophy; yet, after one week of cortisone administration they walked, got on and off chairs and climbed stairs with ease.

The over-all subjective and objective improvement was progressive and was greater with each successive day of cortisone administration, but apparent sudden increases in functional capacity often surprised both the patient and the observers. For example, because of pain on weight-bearing, patient 4 had restricted his walking to the distance between the bed and the toilet. On the fifth day of administration of cortisone he awakened with the urge to walk and proceeded to walk up and down the hospital corridors several times. Before receiving the drug, another patient (case 2) was so dis-

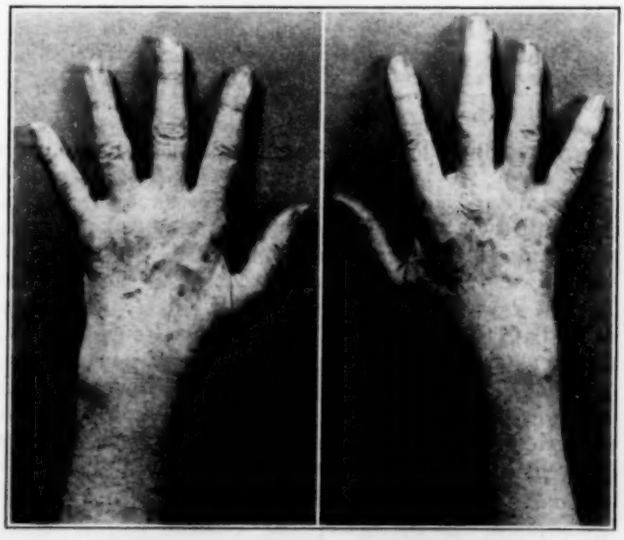

Fig. 2 (case 5).—Appearance of hands of the patient after eight days of administration of cortisone (total dose of 1 Gm.). Joint swelling decreased notably, particularly in the metacarpophalangeal and proximal interphalangeal joints.

abled that she could not get on or off the bed pan without aid from an attendant. Although her improvement had progressed rapidly, she remained cautious about undertaking new adventures—yet on the seventh day she literally danced a jig to the amazement of a group of observers. Although 3 of the 5 patients showed extremely remarkable improvement, they were by no

means entirely free of subjective and objective musculoskeletal manifestations at any time during the short term study. Swelling and tenderness of joints, restrictions of motion and pain on forced motion, although greatly lessened, were still present. Rest pain completely disappeared in 3 patients, but some degree of stiffness of joints and muscles persisted in all, especially in the early morning.

Effects on Constitutional Symptoms.—A rapid change in mental attitude was one of the outstanding improvements noted. Each patient was mentally depressed to some degree before receiving cortisone, and 4 of 5 were pessimistic as to their futures. Within twenty-four to forty-eight hours after administration of cortisone was begun, each patient became cheerful and optimistic. In 3 patients frank euphoria developed, and a psychiatric consultant considered 1 patient "almost hypomanic." This mental stimulation was sufficient to produce mild insomnia in 4 cases, but, despite the lack of sleep, fatigue did not result. To us the mental stimulation appeared to be greater than would be expected on the basis of relief from pain alone. Decided increases in general strength and endurance were noted by all. One patient (case 2) who had a daily fever (100.6 to 102 F.) became afebrile on the second day of administration of cortisone and remained so until two days after administration of the drug was stopped. Within twenty-four to seventy-two hours definite increases in appetite occurred. The appetites became ravenous in 3 patients, and extra quantities of food had to be provided for them. Four of the 5 patients, showed significant gains in weight, varying from 2¼ to 12½ pounds (1 to 5.7 Kg.) during periods of eight days. The fifth patient was on a measured diabetic diet and gained only ½ pound (0.23 Kg.), but his relish for food improved considerably.

Course After Discontinuance of Cortisone.—After withdrawal of cortisone, the clinical manifestations returned to approximately their original severities in 4 of the 5 patients: rapidly in 1, and slowly in 3. In 1 patient (case 1) improvement began to wane within thirty-six hours, and there was an acute exacerbation followed with severe pain, swelling, redness and limitation of motion in several joints; within one week the articular observations and the mental depression were worse and the sedimentation rate was slightly higher than before cortisone was begun. In the other 3 patients increases in rest pain, stiffness, joint swelling and limitation of motion began within two to six days; gradually, over periods of three to six weeks, the overall disability had returned to the precortisone level. Erythrocyte sedimentation rates rose more slowly, but within two months they had returned close to their original values (table).

The fifth patient (case 2), whose disease was the severest and most active, has retained, two months after discontinuance of cortisone, approximately 75 per cent of her maximal improvement.

Toxic Reactions.—Toxic reactions were not noted from the short term administration of cortisone to patients in this series. However, much more experience is needed before definite statements can be made as to the safety of prolonged administration of the preparation, especially in large doses.

SUMMARY OF LABORATORY EFFECTS OF CORTISONE

Erythrocyte Sedimentation Rates.—Sedimentation rates decreased significantly in each of the 5 cases; decreases varied from 15 to 75 mm. within eight days (table). The degree of clinical improvement was not necessarily reflected by the reduction in sedimentation rate. In fact, 2 of the 3 patients (cases 1 and 5) who displayed the greatest clinical improvement had the smallest reductions in sedimentation rates.

Summary of Effects of Cortisone Acetate in Severe Rheumatoid Arthritis

		Clinical Effects with and Following Administration of Cortisone *						Erythrocyte Sedimentation Rates (Mm. in 1 Hour, Westergren Method)		
Case	Sex	Onset of Improvement (Hours After Initial Injection)	Rate of Improvement	Degree of Improvement at Height of Response (8th Day)	Onset of Relapse (Hours After Withdrawal)	Rate of Relapse	Degree of Improvement Maintained 2 Mo. After Withdrawal	Before Cortisone	Height of Improvement (8th Day)	2 Mo. After Cortisone Withdrawal
1	M	10	Rapid	Decidedly pronounced	36	Rapid	None (worse)	74	49	70
2	F	24	Rapid	Decidedly pronounced	See text	See text	75%	128	53	44
3	M	72	Relatively slow	Moderate	96	Slow	None	70	34	74
4	M	36	Fairly rapid	Pronounced	48	Relatively slow	None	97	56	78
5	F	6	Rapid	Decidedly pronounced	48	Relatively slow	None	80	59	77

* Administered in large doses for eight days.

Erythrocyte Count and Hemoglobin Determinations.—Hypochromic anemia, a factor in all 5 cases, was mild in 3, moderate in 1 and severe in 1. Despite daily removal of 30 cc. of blood for laboratory tests, the anemia was significantly improved during the eight day period of administration of cortisone in 3 cases. In these the increases in erythrocyte counts ranged from 390,000 to 930,000 cells per cubic millimeter, and the hemoglobin increases ranged from 0.9 to 2.4 Gm.

Electrocardiograms.—Electrocardiograms taken before and at the termination of administration of cortisone failed to show significant changes except for a slowing of the heart rate, which ranged from 14 to 21 beats per minute in 4 patients. In 1 patient who was febrile before and afebrile during administration of the drug, the decrease was 58 beats per minute. Hench and colleagues noticed a similar heart-slowing effect from cortisone in cases of rheumatic fever.[14]

Electroencephalograms.—Because of the notable mental stimulation which resulted in the first 3 cases,

14. Hench, P. S.; Slocumb, C. H.; Barnes, A. R.; Smith, H. L.; Polley, H. F., and Kendall, E. C.: The Effects of the Adrenocortical Hormone 17-Hydroxy-11-Dehydrocorticosterone (Compound E) on the Acute Phase of Rheumatic Fever: Preliminary Report, Proc. Staff Meet., Mayo Clin. **24**: 277-297 (May 25) 1949.

in 2 of which the patients exhibited frank euphoria, electroencephalographic studies were made before and after the administration of cortisone in cases 4 and 5. In both instances tracings made at the termination of the administration of cortisone revealed increases in frequency of the alpha waves, an increase of 8.8 per cent in 1 and 9.2 per cent in the other. These observations suggest that administration of the endocrine substance may cause a speeding up of cerebral activity.

Dextrose Tolerance.—Intravenous dextrose tolerance tests were made in 2 nondiabetic patients before and at the termination of administration of cortisone. In 1 patient there was no significant change; in the other the tolerance was slightly reduced.

Patient 3 had coexisting diabetes mellitus, which was controlled by a measured diet and 10 units of protamine zinc insulin daily. Administration of cortisone resulted in a temporary intensification of the diabetes. On the second day the insulin requirement increased, and thereafter 30 to 50 units daily were needed to control the disease. Three days after administration of the endocrine preparation was discontinued, the insulin requirement dropped to the precortisone amount of 10 units. Experience in this case indicates that cortisone should be given with extreme caution to patients with diabetes mellitus. Fortunately, the association of rheumatoid arthritis and diabetes is uncommon.

In a separate report certain special laboratory and metabolic studies will be presented.

EFFECTS OF SMALLER DOSES OF CORTISONE ON MILD AND MODERATE RHEUMATOID ARTHRITIS

Although Hench, Kendall, Slocumb and Polley found that doses of 25 to 50 mg. of cortisone were inadequate in severe and moderately severe rheumatoid arthritis, it was logical for them and us to speculate that perhaps smaller doses of cortisone might be effective in controlling mild and relatively mild disease. If further investigation justifies the use of the preparation as a therapeutic agent, this appears as a practical and important consideration because the compound promises to be scarce and expensive in the immediate future. Further, if toxic manifestations should be met with prolonged administration, then theoretically they should be encountered less frequently with smaller doses. Limited supplies of the compound permitted only 3 pilot experiments, but the results in these were promising.

Two patients with moderate and 1 patient with mild but definite rheumatoid arthritis were given 50 mg. of cortisone daily (for ten to fifteen days) until the clinical manifestations had subsided almost completely and the sedimentation rates had returned to normal. Thereafter doses of 50 mg. of the agent were given every other day for twenty-one days.

REPORT OF CASES

CASE 1.—G. H., a housewife aged 44, had chronic rheumatoid arthritis of two years' duration. The articular manifestations were restricted to a few joints: both wrists, the second right proximal interphalangeal joint and the second and fifth metacarpophalangeal joints of both hands, which were moderately swollen, tender and painful on motion. The left ankle was moderately swollen and painful on weight-bearing. Constitutional symptoms were mild, and the erythrocyte sedimentation rate prior to administration of cortisone was 35 mm. in one hour.

Fifty milligrams of cortisone were given daily for ten days. On the second day mental stimulation and a sense of well-being developed. On the third day stiffness and rest pain began to subside, and on the fifth day significant reductions in joint tenderness and swelling were apparent. Improvement continued, and by the tenth day all objective signs had disappeared except for slight tenderness of the fifth right metacarpophalangeal joint and slight residual thickening of the second and fifth metacarpophalangeal joints of both hands. Slight stiffness of the fingers when the patient awakened each morning, lasting for approximately ten minutes, was the only subjective complaint which remained. The erythrocyte sedimentation rate was reduced from 35 to 16 mm. in one hour. The dosage was now changed, and 50 mg. of the compound were given every other day for a period of two weeks. During this period symptoms and objective manifestations gradually returned. The patient experienced also two bouts of acute joint swellings (on the fourth and fifth days), each lasting from twenty-four to thirty-six hours. The erythrocyte sedimentation rate increased to 29 mm. in one hour. The initial dosage of 50 mg. of cortisone daily was reinstituted and continued for ten days. Again the clinical manifestations receded rapidly, and by the fourth day the improvement equaled that attained originally. The erythrocyte sedimentation rate was decreased to 11 mm. in one hour on the tenth day. A dosage of 50 mg. of the preparation given every other day was instituted for the second time and continued for three weeks. During this period joint stiffness and tenderness gradually increased and the sense of well-being lessened. Although the patient was still greatly improved, the disease was not controlled as adequately as it had been when daily doses of 50 mg. of cortisone were given.

CASE 2.—K. W., a housewife aged 49, had typical clinical manifestations of rheumatoid arthritis for four months; during this time she experienced moderate general constitutional symptoms. Before the administration of cortisone the objective manifestations were restricted to five joints: the right wrist and the second and third metacarpophalangeal joints of the left hand were moderately swollen, tender and limited in motion; and both ankles were moderately swollen, tender and painful on weight-bearing. The erythrocyte sedimentation rate was 44 mm. in one hour.

Cortisone was given in doses of 50 mg. daily for fifteen days. All subjective and objective manifestations subsided by the eleventh day except for mild aching, stiffness, limitation of motion and moderate pain on forced motion of the right wrist. After fourteen days the only residual symptom in this joint was slight pain at the extremes of motion. The erythrocyte sedimentation rate was reduced to 12 mm. in one hour. The dosage of cortisone was then decreased to 50 mg. every other day and continued for three weeks. The ankles and metacarpophalangeal joints remained objectively normal and asymptomatic. Aching, stiffness and pain on forced motion of the right wrist increased slightly, mental stimulation lessened and the erythrocyte sedimentation rate increased to 30 mm. in one hour.

CASE 3.—E. M., a woman aged 42, had experienced aching and stiffness in various peripheral joints and recurrent swelling in the proximal interphalangeal and metacarpophalangeal joints of the hands for approximately three years. For three months prior to the administration of cortisone the symptoms were more pronounced and persistent swelling developed in the fourth and fifth proximal interphalangeal and the second and fifth metacarpophalangeal joints of the right hand. The right wrist was moderately swollen, tender and painful on forced motion. Moderate constitutional symptoms, particularly fatigue and anorexia, had been present for three years. The erythrocyte sedimentation rate was 26 mm. in one hour.

Cortisone was administered to the patient in 50 mg. doses daily for twelve successive days. By the fifth day the constitutional symptoms disappeared; she felt "full of pep" and began to go out socially during the day as well as at night. By the tenth day joint swellings had entirely subsided and the only remaining objective manifestation was slight tenderness on deep pressure of the right fifth metacarpophalangeal joint. Subjectively her only complaint was mild early morning stiffness of the fingers, lasting approximately thirty minutes. The

erythrocyte sedimentation rate was diminished to 6 mm. in one hour by the twelfth day. The dose of cortisone was then reduced to 50 mg. every other day and continued for three weeks. Except for increase in morning stiffness, the initial improvement was retained.

Definite conclusions cannot be drawn from short term studies in 3 cases. However, results suggest that smaller doses of cortisone, 50 mg. daily or perhaps less in some cases, may be sufficient to control adequately cases of mild and moderate rheumatoid arthritis. Whereas the clinical manifestations subsided almost entirely with daily injections of 50 mg. of the compound, there did remain some residue of the disease, even though slight, in each case. This indicated that the patients were not entirely well and that, although the disease was greatly suppressed, complete remissions had not been invoked. The clinical manifestations were not controlled as well when the dose of cortisone was reduced to 50 mg. every other day. Before the administration of cortisone each patient was somewhat depressed mentally. With doses of 50 mg. of the agent a day each became mildly euphoric and acquired a sense of well-being which was greater than normal. With reduction of the dose to 50 mg. every other day, euphoria disappeared but depression did not recur; mentally each patient felt "about normal."

SUMMARY

The adrenal cortical hormone, cortisone acetate (compound E acetate: 17-hydroxy-11-dehydrocorticosterone acetate) was administered for short or relatively short periods to 8 patients with rheumatoid arthritis. Definite, but temporary, improvement in the clinical and certain laboratory features of the disease resulted in each case.

Five of the eight patients had severe rheumatoid arthritis and were given large doses of cortisone acetate for short periods (total of 1 Gm. in divided doses for eight days). The immediate results were decidedly pronounced improvement in 3, pronounced improvement in 1 and moderate improvement in 1. Prompt or fairly prompt relapse of the disease, with return of clinical manifestations approximately to their original severities, occurred after withdrawal of the endocrine preparation in 4 of the 5 cases. The fifth patient retained, 2 months after discontinuance of the use of cortisone, approximately 75 per cent of the initial improvement.

Three additional patients with less severe rheumatoid arthritis (2 with moderate and 1 with mild disease) were given smaller doses of the drug for longer periods. With daily doses of 50 mg. the symptoms and objective observations were adequately, but not completely, controlled. Doses of 50 mg. of cortisone acetate given every other day were not as effective in controlling the clinical manifestations.

Because of the small number of cases reported and the brief periods of administration of cortisone, definite conclusions cannot be drawn. However, the results in 8 cases indicate that this adrenal cortical preparation, when given in large or relatively large doses, will rapidly suppress the clinical manifestations of rheumatoid arthritis. The results reported herein confirm the observations made originally and described recently by Hench, Kendall, Slocumb and Polley.

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THE FAMILY DOCTOR

An Epidemiologic Concept

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The picture of the family doctor has been drawn by greater artists than I. In his role as confidant and confessor, busy but patient, sometimes limited in preparation but long in understanding, he created a position which deeply influenced the decisions of the family and community. Through long and intimate acquaintance he learned the social and economic stresses of his flock, the hidden errors and the familial blights to be encountered. He encouraged the promising and helped cushion the realities and failures of the less successful. His position as sociologist and practical psychologist has not been filled in the community, for the industrial revolution and the present industrial revolt have changed the atmosphere of the growing community from one of neighborly sharing in the intimate pleasures and problems to one in which sociologic interest is too largely official and too often accompanied with political aspirations. The vanishing of this priesthood has been hastened by the times rather than by medical progress. However, Davis Riesman,[1] in his excellent essay on the family physician, points out that the results of preventive medicine, the rise of specialism in medicine and the great advances in laboratory aids—all of which I ascribe to the times—have tended to eliminate the doctor of the old school. One other feature is important: the less frequent visiting by the doctor at home, where the environment could be sensed and other members of the family would be encountered. It is my purpose not to attempt an analysis of all the contributing influences but at this point to accept the fact that the family doctor, the servant and preceptor of the community, as traditionally immortalized in fact and fiction, has been slowly retiring before current trends.

However, the changing scene has not been without its recompense. The understanding of disease as a problem interpretable in terms of the community has been greatly advanced by the combination of ecologic, clinical and laboratory investigations. And it is for this reason that I should like to reestablish the modern physician as the family doctor, employing the available evidence of the role of the family as a unit of disease. The epidemiologic outlook affords a basis for early identification of the abnormal and by anticipating the situation permits more effective maintenance of health and the application of preventive medicine.

THE FAMILY

The family can be considered in different perspectives. As a household ". . . it includes the related family members and also the unrelated persons, such as lodgers, servants or hired hands," [2] and, for the purposes of this paper, the attached flora and fauna. In other words, this is a group brought together under communal conditions, sharing the same facilities for the ordinary purposes of life. Although officially insti-

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1. Riesman, D.: Medicine in Modern Society, Princeton University Press, 1939, p. 145, Princeton, New Jersey.
2. Population Characteristics, Series P-20, no. 16, Bureau of Census, United States Government Printing Bureau, May 5, 1948.

tutions, barracks or camps do not constitute households, they do represent epidemiologic families by virtue of the common life of their occupants.

The other concept of a family is that based on blood or marital relationship. In these circumstances the genetic factor is the one of interest, extending beyond a single household and even into several generations. The blood lines and their accompanying peculiarities may thus be of greatest importance to the thesis of this article.

The rate of migration and the well defined individuality of present day life have served to disrupt the continuity of the family as a unit in a given community as well as to reduce the probability that a single physician could keep the group under observation for an extended period. Even the official health agencies have specialized the family through divisions such as maternal and child health, school health and industrial health, instead of a total approach to family health. Despite this decreased opportunity to supervise the entire family, accumulated information now allows the physician who sees but a single member of the family in distress to state probabilities as to the status of the others and thus serve the family as a whole. The role of psychologist has been amply stressed by others, and I shall elect to suggest the broader function in organic disease.

EXAMPLES FROM INFECTION

In the field of infection physicians are increasingly confronted by the fact that the case of what is termed the typical disease is so likely to be the incident or accident of group infection. It is commonplace that meningitis is a random accident in the course of infection with Meningococcus and that a large proportion of intimate associates of the patient may be infected with the same organism without displaying significant signs of disease. So, too, with the patient whose lobar pneumonia is due to type I Pneumococcus. A majority of the other members of the family may be infected with the same organism. They may present little clinical evidence of illness or may have what passes for a cold or a mild sore throat—or apparent otitis or sinusitis. The case of pneumonia is the accident. The family represents a concentration of infection of continued risk to itself and to the community.

The problem of streptococcic disease has been largely dominated by clinical terminology, but now it is clearly seen that within the infected group the same organism may be associated with a wide range of reaction, from the subclinical infection, through frank disease, to the secondary phenomena of rheumatic fever and acute nephritis. In this instance, again, the clinical case may be the exceptional feature acting to turn the spotlight on the probability of a highly infected group. Granted that it is not at present practicable accurately to determine the duration of the individual infectiousness of each member, it is equally undesirable to ignore the risk which such groups offer to the rest of the population. Although the studies of Hamburger and others have largely been conducted in barracks or hospital wards, their demonstration of the high contaminating potential of the chronic nasal carrier would seem readily applicable to school room or occupational groups.

Hence, whether seen in the office, the clinic or the hospital, observation of a patient with a frank case of disease due to the aforementioned agents should call the attention of the physician to the family, with the purpose of limiting the spread or the severity of infection among the individual members, of reducing the possibility of chronic sequelae and of cutting down the danger to the community.

The approach indicated here has been so completely applied in the control of typhoid and tuberculosis as to constitute the major attack. For example, the studies of Ramsey [3] and of Stebbins and Reed [4] in the state of New York have demonstrated that the probability of contracting typhoid was from 1,200 to 1,900 times greater in a familial associate of a patient with the disease than in the general population; that the incidence of typhoid among familial associates of a carrier was 42 times greater than in the general population. To state it another way, 7 per cent of familial associates of patients with typhoid contracted the disease, and the poorer the sanitary facilities the higher the rate. The actual data for infection would undoubtedly be greater, because a considerable portion of persons so exposed may undergo active infection without having their disease diagnosed as typhoid.

The detection of tuberculosis by study of the familial associates of patients with identified disease is the most productive method, even though the extensive programs tend to miss the adult members who contribute the greatest number of cases. The closer the association with a tuberculous patient in the household, the greater the frequency of infection and disease.[5]

The intensity of family infection can be further illustrated by two virus diseases, poliomyelitis and infectious hepatitis. Although it continues to be said that more than 1 case of poliomyelitis in a family is unusual, it has been clearly demonstrated that the probability of an additional paralytic case in a family in which one has already appeared may be 25 times greater than the incidence in the rest of the population. Our 1943 studies in Texas [6] and those of Gordon and his associates in Chicago [7] reveal that the frequency of virus infection among familial associates, as measured by the demonstration of virus in stools, may be 30 to 40 times greater than that among those without known association with the disease. Furthermore, these positive observations represent active infections, readily acquired. For instance, in the study of a family, by Zintek of this department,[8] it was found that four days after all specimens from a family were negative for poliomyelitis virus, a case of nonparalytic disease occurred in the family and that in another five days 2 more cases had occurred and virus was present uniformly in the stools of the parents and the children, and in the throats of the children. Furthermore, 3 of 4 members of the family continued to show virus in the stools when tested three weeks later. Additional evidence of the continued infection is seen in the studies made in four families from Detroit.[9] Most of the children were infected, 3 of them yielding consistently positive stools for four to five weeks. Although in this

3. Ramsey, G. H.: Typhoid Fever Among Household Contacts with Special Reference to Vaccination, Am. J. Hyg. **21**: 665, 1935.

4. Stebbins, E. L., and Reed, E.: Carrier-Borne Typhoid Fever in New York State with Special Reference to Attack Rates Among Household Contacts, Am. J. Pub. Health **27**: 233, 1937.

5. Chadwick, H. D., and Pope, A. S.: The Modern Attack in Tuberculosis, New York, The Commonwealth Fund, 1942, p. 63. Opie, E. L.: Tuberculosis Infection in Children and Adults; Relation of One to the Other, J. Outdoor Life **24**: 274, 1927.

6. Pearson, H. E.; Brown, G. C.; Rendtorff, R. C.; Ridenour, G. M., and Francis, T., Jr.: Studies of the Distribution of Poliomyelitis Virus: III. In An Urban Area During an Epidemic, Am. J. Hyg. **41**: 188, 1945.

7. Gordon, F. B.; Schabel, F. M., Jr.; Casey, A. E., and Fishbein, W. I.: Laboratory Study of the Epidemiology of Poliomyelitis, J. Infect. Dis. **82**: 294, 1948.

8. Zintek, A. R.: The Rapid Infection of a Family After Introduction of Poliomyelitis Virus, Am. J. Hyg. **46**: 248, 1947.

9. Brown, G. C.; Francis, T., Jr., and Ainslie, J.: Studies of the Distribution of Poliomyelitis Virus: V. The Virus in Familial Associates of Cases, J. Exper. Med. **87**: 21, 1948.

series the apparently well adults did not yield virus, 2 of the 4 clinical cases occurred in adults. Moreover, in other studies the persistence of subclinical infection among the associated familial adults has been amply demonstrated.

Infectious hepatitis, formerly designated catarrhal jaundice, is again a virus infection in which the group

Fig. 1.—Familial distribution of 70 cases of infectious hepatitis.

characteristics of the infection are prominent. Its eruption in institutions, military units and camps is well known, but all too often in the general population the physician may see only the apparently sporadic case. Pickles, in his charming exposition of "Epidemiology in Country Practice," [10] has followed in his community of practice the familial distribution of that disease. To illustrate the familial concentration I would refer to an epidemic studied by the staff of the Epidemiology Department [11] in 1944 in Central Michigan in a population of essentially 400 persons. Thirty-three families consisting of 155 persons were involved; of these 75, or 44 per cent, had infectious hepatitis and in twenty families multiple cases occurred. The largest family of 10 persons had 7 cases, including the only fatality. The primary cases centered about the village school, embracing the age group of 5 to 10 years; 45 of the 61 children so exposed became ill (figs. 1 and 2). In only 6 instances did the first case observed in a family occur in another age group, and even then there had been some close association with the school and its children. The subsequent dissemination in the families emphasizes the concentration of infection in families to which the infected school child belonged. It emphasizes, too, that in infectious hepatitis there is a large body of concealed infection and suggests that recognition of a single case of hepatitis with jaundice should center attention on the infected family.

10. Pickles, W. N.: Epidemiology in Country Practice, Baltimore, Williams & Wilkins Company, 1939.
11. Unpublished data.

Examples from the field of infection could be multiplied to cover a wide range of mechanisms of transmission and the influences of environment, as with brucellosis and the farm household. The minor foibles, habits and taboos of the family often result in their exposure to agencies which would not otherwise give rise to group disturbances. The familial concentration of pellagra is a striking evidence of the effect of familial habits on the health of the unit.

EXAMPLES IN METABOLISM

Turn now to the genetic family. The instances of developmental and anatomic aberrations of an inheritable nature are manifold, and recognition of them promptly calls attention to the possibility of their presence in other members of the family. Certain of the blood dyscrasias clearly follow a genetic pattern.

It seems evident, also, that genetic influences may play an important role in the responses of certain family groups to infection. Rheumatic fever is a case in point. There is a familial tendency toward aggregation of this disease in family clusters, while other families apparently undergo the same experiences without that result. Still other families appear to be relatively resistant to streptococcic infections at any level. The rheumatic family has been studied, from the genetic point of view, especially by Wilson,[12] who concluded that hereditary susceptibility underlies the familial incidence of the disease. One may suggest that this, too, could represent a defect in the metabolic process required for disposal of certain products of streptococcic infection. St. Lawrence [13] in 1922 stated the problem on the basis of his familial studies: ". . . from the facts at present available no conclusions can be reached as to the relative importance of inherited susceptibility and dissemination by close contact between infected and noninfected persons." Again, ". . . it would seem imperative that physicians, on discovery of rheumatic infection or cardiac disease in one member of a family, should strongly recommend the examination of all other members of that family for evidence of these conditions. . . . the 'family group' will assume increased signifi-

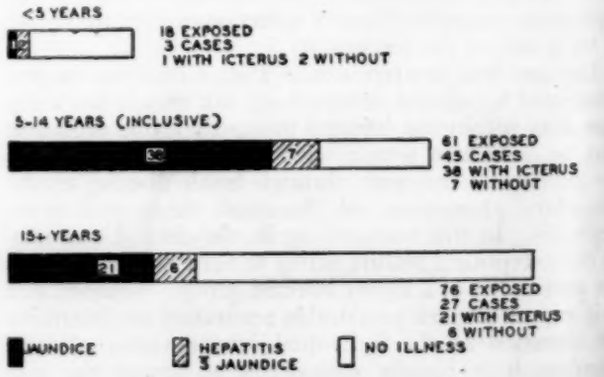

Fig. 2.—Incidence of illness in exposed families by age groups (75 cases).

cance in the dissemination of rheumatic infection, and therefore of cardiac disease, and offer an important place for the intensive application of such preventive measures as are available."

But of particular interest are those established disturbances of metabolism which are also genetic in

12. Wilson, M. G.: Familial Epidemiology of Rheumatic Fever, in Rheumatic Fever, New York, The Commonwealth Fund, 1940, chap. 3.
13. St. Lawrence, W.: The Familial Association of Cardiac Disease, Acute Rheumatic Fever and Chorea: A Study of a Hundred Families, J. A. M. A. 79: 2051 (Dec. 16) 1922.

character. Allergy may be one of them. Diabetes and thyroid disturbance are others. Since they may have a definite relationship to the aging process and vascular degeneration, attention is called to those associated with lipid metabolism. In the case of xanthomatosis, or hypercholesterolemia, the cutaneous lesion is sufficient to direct investigation to a widely distributed metabolic disturbance in the family. There is increased interest because these abnormalities are associated with coronary sclerosis and cardiac death before maturity. Wilkinson, Hand and Fliegelman [14] have reported a study of 282 members of a family in four generations. Of these, 159 were thoroughly investigated and 30, or 20 per cent, were found to have hypercholesterolemia; 3 of them died sudden, presumably cardiac, deaths before the age of 20. Bloom, Kaufman and Stevens [15] reported a family in which 4 children died of coronary disease at the ages of 23, 18, 14 and 6½ years. There are many examples in which some obvious clinical lesion can indicate a broad familial defect, which could be explored with profit to the health of the family.

THE PLAN OF ACTION

The observation that disease might run through a family or an intimate group is as old as disease itself, and the realization that there is considerable variation in the response of different members of the group is also of long standing. Moreover, with the advent of the bacteriologic era the importance of the clinically unrecognized and of the carrier infection became apparent as sources of risk. Chapin [16] and Frost [17] emphasized the study of the family group for a measure of the transmissibility of disease in terms of the secondary attack rate. And it is certain that with the advent of diphtheria antitoxin for prophylaxis the family physician came rapidly to realize that the frequency with which the disease might run through families could be sharply reduced.

With that exception, however, there was little to offer but isolation and quarantine. And the effectiveness of these latter procedures has been so limited by economic demands and by the inability to apprehend a large proportion of infected persons that the measures have come to be considered of little value. Nevertheless, in tuberculosis the opposite view of isolation is strongly maintained. There is an important contradiction in this behavior. It is apparent in many of the infections that association with the frank case of disease does not account for the majority of new cases. The missed case and the carrier therefore are accepted as definite hazards. Some authorities tend, however, to ascribe much of the importance in dissemination to the acute stage of the missed case while minimizing the role of the carrier, who is in reality an example of active acute infection. This seems to be an exercise in semantics. The more acute the disease the less readily are the missed case and the inapparent infection differentiated. The carrier of the enteric organisms is accepted as a constant risk if he is provided opportunity to effect the transfer of his organisms. The tuberculous patient who continues to put out organisms is a recognized hazard. The patient with streptococcic sinusitis is a remarkably rich source of infection, whether he is in the early febrile stage or not. The term carrier tends to connote a passive acceptance of organisms, but properly it should be realized that where the organisms are maintained they multiply and the host is infected. He may follow a course of infection comparable in terms of microbial growth to that of the frank case, leading finally to elimination of the agent or to chronic infection. To return, then, to the traditional "case of disease" in the family; since it is realized that it commonly represents the crop line of a greater bed of infection in the family cluster, should not this unit of greatest density of infection be treated as a group of acute infections? It is difficult to accept the idea that to permit these persons with active infections to move freely without some effort to erect a barrier between them and the susceptible members of the community can do other than increase the dissemination.

The progressive availability of drugs and antibiotics against a wide range of infectious agents offers a new hope in this respect. The efficacy of small doses of sulfonamide compounds in curing the subclinical infections caused by meningococci immediately recommends their employment in any familial unit in which a case of meningitis of that nature occurs. The influence of sulfonamide drugs and penicillin on pneumococcic and streptococcic infections of the upper respiratory tract is less dramatic, but there is sufficient evidence to indicate that a bacteriostatic effect can be obtained or that initiation of infection can be avoided. In the Salmonella infections, chloramphenicol (chloromycetin®); in the dysenteries, sulfonamide compounds; in infectious hepatitis, gamma globulin may be used. For poliomyelitis there is no specific prophylactic or therapeutic agent to be recommended. Nevertheless, as has repeatedly been emphasized, if control measures are to reduce the spread of that disease from one person to another, the families of the patients with recognized cases constitute the units exhibiting the greatest density of infection toward which attention should be strongly directed.

It is not intended to urge that present products be used indiscriminately or without weighed judgment; the objective of limiting the course of infection and reducing the density of infection in the community is the important concept. Too often the physician is guilty of treating the individual patient; too commonly public health authorities are guilty of concentrating on the number of cases, and the administrative approach is too largely governed by severity of disease. No one knows how much the degenerative disturbances of later life are related to the effects of the simple diseases of childhood. Without concern for the future of naturally acquired immunity, active prophylaxis seems desirable, and as prophylaxis increases experience has repeatedly proved that the risk of infection in the community declines.

SUMMARY

The purpose of this article has been to emphasize the fact that the present day physician can become once more the family doctor, whether he sees the patient at home, in the office or in the hospital, by the use of epidemiologic data such as have been presented. Moving along the lines suggested, he can advance as a conservator of health and in the promotion of preventive medicine. By continued recording of the distribution of disease in the families and in the community he serves, the physician can add greatly to progress in the field of epidemiology and constantly function in the foreground of efforts toward the control and elimination of disease.

14. Wilkinson, C. F., Jr.; Hand, E. A., and Fliegelman, M. T.: Essential Familial Hypercholesterolemia, Ann. Int. Med. **29**: 671, 1948.
15. Bloom, D.; Kaufman, S. R., and Stevens, R. A.: Hereditary Xanthomatosis, Arch. Dermat. & Syph. **45**: 1 (Jan.) 1942.
16. Chapin, C. V.: Report of Commissioner of Health of Providence, Rhode Island, 1903-1905.
17. Frost, W. H.: The Familial Aggregation of Infectious Disease, Am. J. Pub. Health **28**: 7, 1938.

MODIFIED PROTAMINE INSULIN (NPH-50)

A Clinical Report

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This article is a clinical report on the use of modified protamine insulin (NPH-50)—first, what it is; second, why it is indicated; third, how does it differ from present market insulins; fourth, what has been the experience of the Joslin Clinic in its use; fifth, what technics have been employed in its administration, and, sixth, what are its failures as well as its successes?

Insulin of the NPH-50 type contains protamine modified by crystallization. Neutral in reaction, it is designated N; protamine, it is termed P; improved by Hagedorn, it is named H; modified by the addition of 0.50 mg. of crystallized protamine for every 100 units of insulin, it is tagged 50—therefore, NPH-50 insulin.

New modifications of insulin are being and should be sought. Wonderful though insulin is, the forms now available have three obvious defects; first, their administration is parenteral; second, their time of action is too slow, too short or too long, and third, their hypoglycemic effect may be of abnormal degrees. The ideal insulin has been defined by Best and by Hagedorn as depot in type and one which releases insulin as tissue sugar rises and withholds it as tissue sugar falls, thereby controlling hyperglycemia and preventing hypoglycemia. Since this ideal insulin of the physiologist is not available, clinicians clamor for an insulin practical in nature with instant availability and with twenty-four hour action. Modified protamine insulin has some of the desired clinical properties.

The blood sugar lowering action of modified protamine insulin is relatively quick, because it begins some two hours after administration compared with one hour for regular and crystalline, one to two hours for globin and six to eight hours for protamine zinc insulin. The maximum blood-lowering action occurs some ten to twenty hours after administration compared with three hours for regular and crystalline, six hours for globin and twenty-four hours for protamine zinc insulin. The duration of action is long, namely, twenty-eight to thirty

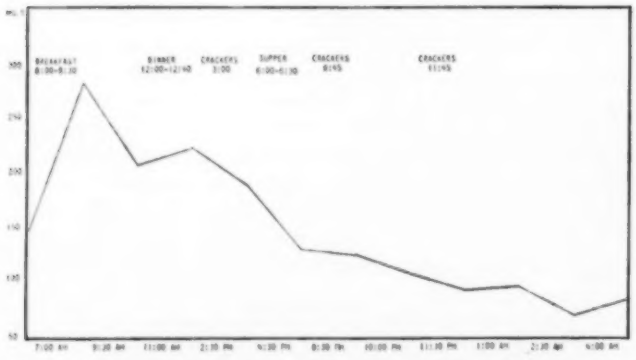

Chart 1.—Composite curve of levels of capillary blood sugar of 7 patients receiving modified protamine insulin (NPH-50) on a typical camp day.

hours, compared with six and eight hours for regular and crystalline, respectively, fifteen for globin and up to seventy-two hours for protamine zinc insulin. In mixtures the modified protamine insulin adsorbs less of added crystalline insulin than does market protamine zinc insulin. The greater degree of adsorption by protamine zinc insulin occurs because it contains 1.25 mg. of protamine for every 100 units of insulin, in contrast to 0.50 mg. in the modified preparation.

Insulin of the modified protamine type is therefore relatively quick in action, for it lags two hours only,

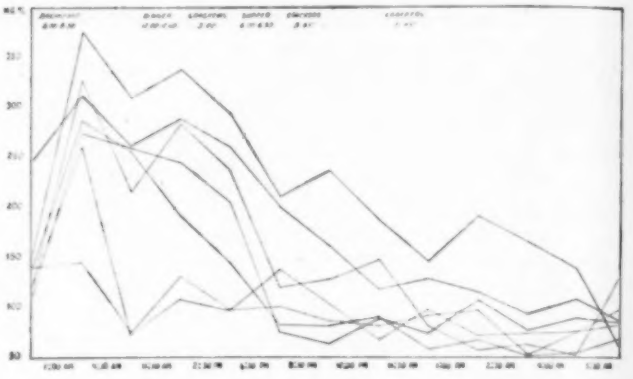

Chart 2.—Individual curves of levels of capillary blood sugar of 7 patients receiving modified protamine insulin (NPH-50) on a typical camp day.

has long duration of action—some twenty-eight hours—and has nocturnal hypoglycemic hazard rather than the more dangerous daytime hazard. From this description it is evident that the modified protamine insulin resembles the popular 2:1 mixture of crystalline and protamine zinc insulin.

Between June 1948 and June 1949, 336 patients of the Joslin Clinic were treated with modified protamine insulin.[1] This group consisted largely of patients whose diabetes was characterized by its severity and in whom chemical control had been difficult. The majority, 260, were patients under the age of 20 years and the other 76 were adults. The group of patients under 20 years of age were taken consecutively from the clinical material. The choice of the adults was a selective one; obstetric patients with diabetes comprised 21 of the number, and the 55 others were chosen because of great sensitivity to insulin. In addition to the 336 patients, comparison studies were made by Dr. Alexander Marble on a group of patients whose diabetes was mild and who were hospitalized for their surgical complications. The series of 336 patients is overloaded with young diabetic persons because severity and lability characterize juvenile diabetes, and experiences with them can be used as a therapeutic guide in all patients whose diabetic management is difficult.

Adjustments to modified protamine insulin were made, first, at our two summer camp units; second, in the Deaconess Hospital, and, third, in the office. The greatest number (203) of the patients were transferred to modified protamine insulin at the summer camp units. One hundred and twenty-four girls were treated at the Clara Barton Camp under the direction of Dr. Ruth E. Reuting and myself and 79 boys at the Elliott P. Joslin Camp under the direction of Drs. A. J. Gabriele and Alexander Marble. Office regulation was accomplished in 35 patients, and 98 were hospitalized.

Fasting experiments were not conducted; however, after stabilization on the modified protamine insulin a small group of children had capillary blood sugar determinations at approximately two hour intervals on a typical camp day. The Folin micro method was used.

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Read before the Joint Meeting of the Section on Internal Medicine and the Section on Experimental Medicine and Therapeutics at the Ninety-Eighth Annual Session of the American Medical Association, Atlantic City, N. J., June 10, 1949.

1. The modified protamine insulin was supplied by Eli Lilly and Company.

The average curves for the 7 girls (charts 1 and 2) whose blood sugar levels were determined in the morning at 7, 9:30 and 11, in the afternoon at 2:30 and 4:30, in the evening at 8:30, 10 and 11:30 and during the night at 1, 2:30, 4 and 5:30 showed a rise to abnormal values in three periods only; namely, at 9:30 after breakfast, at 11 in the morning and at 2:30 in the afternoon after lunch. The average blood sugar values for the remaining nine periods were all at normal levels. The lowest average occurred at 4 a. m., twenty hours after administration of the insulin. The experience with diabetic boys was similar.

After they had been stabilized with separate injections of crystalline and protamine zinc insulin and again after they had been stabilized with a single injection of modified protamine insulin, the levels of the blood sugar at 7 o'clock (fasting), in the morning at 11, in the afternoon at 4 and in the evening at 8 were determined in 72 girl campers.

The average blood sugar level was lower at each year of age fasting, at 4 p. m. and at 8 p. m., when modified protamine insulin was administered in a single injection; the average blood sugar level for each year of age was lower at 11 a. m. when separate injections of crystalline and protamine zinc insulin were administered. The experience with diabetic boys was similar. In juvenile diabetic campers a single injection of the modified protamine insulin controlled diabetes chemically as well as, if not better than, separate injections of crystalline and protamine zinc insulin.

The adults who had a mild form of diabetes and had surgical complications were transferred readily to modified protamine insulin therapy. Patients of this type, however, do not present difficulties in diabetic management, and the disease can be controlled chemically without difficulty with each type of insulin. Of the insulin-sensitive adults, three quarters of the number were controlled more easily with modified protamine insulin than they were before, but one quarter of them did not show improvement. The seriousness of hypoglycemia in this group cannot be overemphasized. Jobs are at stake, professional judgment is disturbed and the care of young children is a risk.

The results in the obstetric cases were encouraging. Low renal threshold for dextrose characterizes the pregnant diabetic woman and is one of the causes for her susceptibility to ketosis and hypoglycemia. Therefore our scheme for insulin therapy has included separate injections of crystalline and protamine zinc insulin before breakfast, supplemented by crystalline insulin before lunch, dinner and even at bedtime. In 60 per cent of these patients a single injection of modified protamine insulin replaced multiple injections.

Although the evaluation of a new form of insulin should be made on patients under direct medical supervision, practical evaluation of insulin therapy in the diabetic subject must include a survey of the results among patients controlling their own treatment. Therefore clinical success with modified protamine insulin was measured further: first, by the degree of chemical control after the patients were discharged from camp and hospital; second, by freedom from reactions; third, by freedom from bouts of acidosis, and fourth, by the maintenance of proper nutritional levels and by the promotion of normal rates of growth and development. Bouts of coma and reactions of severity were infrequent. Nine, or 3 per cent, of the patients had reactions which required their hospitalization; 3, or 1 per cent, had diabetic coma. Gain in weight and growth in height were superior to previous levels and rates. There was 1 fatality, a cardiac death. The range of 638 random blood sugar levels after discharge was wide, but 40 per cent were below 200 mg. and 70 per cent below 300 mg.. per hundred cubic centimeters. Modified protamine insulin is not a panacea which does away with the need for adherence to diet or for the continuation of insulin therapy.

Comparison of Blood Sugar Determinations After Stabilization with Crystalline, Protamine Zinc and Modified Protamine (NPH-50) Insulin

Age	No. of Cases	Diet at Entrance C.	P.	F.	Cal.	Diet at Discharge C.	P.	F.	Cal.	Weight (Lb.) Entr.	Disch.	Insulin Crystalline	Prot. Zinc	Total Units	Blood Sugar (Mg./100 Cc.) NPH-50	F.	11	Before NPH-50 4	8	F.	11	After NPH-50 4	8
2	1	115	58	64	1268	115	58	64	1268	....	....	6	11	17	26	105	305	305	320	89	270	185	191
3	1	142	68	76	1524	108	75	87	1755	35.0	39.0	10	4	14	34	164	183	283	257	61	261	55	148
5	2	151	74	75	1505	151	74	75	1575	40.3	42.5	11	15	26	37	103	155	130	305	104	150	198	132
6	6	159	74	79	1573	176	81	89	1829	49.5	50	11	13	24	31	117	148	162	211	109	110	149	133
8	6	178	82	89	1841	182	82	88	1848	60.8	61.2	11	18	29	36	208	123	182	253	183	182	176	156
9	9	184	86	99	1971	192	88	92	1948	65.4	65.4	11	26	37	43	150	146	206	248	116	231	179	225
10	6	198	92	95	2015	204	96	96	2004	73.5	74.4	14	16	30	34	135	126	183	206	115	155	168	161
11	8	201	99	100	2100	220	106	107	2267	79.5	82.7	15	26	41	49	127	115	191	317	97	170	115	158
12	8	212	107	106	2230	225	112	109	2329	90.3	92.0	20	39	59	62	162	189	204	209	132	149	183	197
13	7	206	103	102	2154	221	112	108	2304	93.4	95.1	17	32	49	50	127	114	164	205	118	178	132	163
14	6	207	103	101	2149	205	99	97	2089	116.0	117.1	19	58	77	84	164	168	171	227	105	228	188	180
15	7	204	102	95	2079	210	106	99	2155	115.0	114.6	22	47	69	67	171	200	204	290	145	220	148	158
16+	5	200	99	96	2060	209	105	100	2169	119.9	120.9	22	44	66	77	149	104	159	246	109	215	154	169

The technic used for the readjustment from crystalline and protamine zinc insulin to modified protamine insulin was simple. The sum total in units of all previous doses of insulin was given. It was learned quickly that most patients required in units larger doses of insulin in the modified protamine form than in the sum total of crystalline and protamine zinc types. The aim of treatment was freedom from sugar and the maintenance of normal levels of blood sugar.

The most important single test for the regulation of modified protamine insulin, as it is with all long-acting insulins, is the true fasting test, which should be aglycosuric or nearly so. Hyperglycemia and glycosuria occurring at premeal and retiring periods in the presence of a perfect fasting test indicate the need for adjustments other than that of modified protamine insulin, such as reapportioning of the diet. Carbohydrate may be subtracted from the offending meal and added to the diet in the latter part of the day when modified protamine insulin is most effective. The prescription of exercise is also useful. Since little adsorption of quick-acting insulins occurs in mixtures of crystalline and modified protamine insulin, early daytime glycosuria may be prevented by such an addition. Glycosuria occurring in the evening may be prevented by the addition of a supplementary dose of insulin (crystalline) before the evening meal. The addition of rapidly acting insulin was seldom necessary in the group under observation.

The caloric prescriptions commonly used in the Clinic were continued, namely, 30 calories per kilogram of ideal body weight for adults, 30 calories per kilogram of increasing body weight for the pregnant diabetic persons and 1,000 calories for age 1, with 100 added for each year in childhood. The range of carbohydrate was from 150 to 250 Gm. daily. The carbohydrate for breakfast was maintained at a low level, one fifth of the total; one fifth to two fifths were prescribed for lunch and two fifths to three fifths for supper. Midmorning lunches were omitted, but small lunches of 10 Gm. of carbohydrate were given to the children in the afternoon and a lunch of at least 20 Gm. of carbohydrate was given to all patients at bedtime.

The most conspicuous failures with modified protamine insulin occurred in those few patients whose requirement for rapidly acting insulin is great in proportion to that of slowly acting insulin. This is commonly observed in very young diabetic children, among whom unexpected prelunch reactions occurred and severe night time hypoglycemia was not uncommon.

CONCLUSIONS

1. In few instances, only 5 per cent of the patients treated, a single injection of modified protamine (NPH-50) insulin was less successful in controlling diabetes than were separate injections of crystalline and protamine zinc insulin. These few failures included one fourth of the insulin-sensitive adults treated, the majority of the diabetic children under 5 years of age and those patients whose requirements for long-acting insulin are small compared with their requirements for quick-acting insulin.

2. In 95 per cent of the 336 persons with severe diabetes modified protamine insulin was used as successfully as, if not more so, than separate injections of crystalline and protamine zinc insulin.

3. Regulation of diet and exercise is a necessary adjunct to treatment with modified protamine insulin in order to maintain chemical control. With the patient under medical observation it was seldom necessary to add, or supplement with, rapidly acting insulin.

4. Modified protamine insulin combines long duration of action with rapid availability. When administered before breakfast, its hypoglycemic hazard is nocturnal.

5. Modified crystallized protamine insulin (NPH-50) is a desirable insulin for the treatment of severe labile diabetes.

81 Bay State Road.

ABSTRACT OF DISCUSSION

Dr. Cyril M. MacBryde, St. Louis: Many groups of workers throughout the world have continued to study the problem of finding a satisfactory form of insulin which will, with a single injection daily, establish good control of the blood sugar throughout the twenty-four hours. Only one of the intermediate types of insulin, globin insulin, has reached the market. Globin insulin has proved unsatisfactory for the majority of patients with moderately severe or severe diabetes. Another type of modification which has been used is the mixture of crystalline or regular insulin with protamine zinc insulin. There are many possible variations of such mixtures. A superior type of fixed or standard protamine insulin modification was developed, called NP-50 which has 25 per cent of its insulin in solution and 75 per cent in the precipitated protamine insulin component. The blood sugar curves with this insulin modification have in our experience been the most satisfactory that we have been able to get with any type of insulin. This NP-50 insulin differs from the NPH-50 insulin which has been described by Dr. White in that it has 25 per cent of the insulin in solution, whereas in the NPH-50 insulin all the insulin is in precipitated form. It seemed highly desirable to have such an insulin as NP-50 with its biphasic insulin components and good twenty-four hour control of the blood sugar. However, the insulin manufacturer informed us that NP-50 insulin apparently cannot be manufactured in stable form. Therefore, about a year ago the NPH-50 modification was developed and furnished to several groups of investigators for study. The NPH-50 insulin we have studied is the same as the modified protamine insulin on which Dr. White has reported. We agree that it gives a fairly good intermediate type of effect; but the twenty-four hour blood sugar curves with NPH-50 in our hands have not been nearly as good as those obtained with NP-50 insulin. We believe that the NPH-50 modification is not a sufficient improvement over globin insulin, which is now available, to make it advisable that anyone suggest its adoption for widespread use. The NPH-50 insulin, like globin insulin and the 2:1 mixture, controls 75 or 80 per cent of cases of mild diabetes rather well, but in moderate or severe diabetes it has not given sufficiently rapid effect and therefore does not sufficiently control the blood sugar rise after breakfast. It tends to cause low afternoon blood sugar levels. The NPH-50 modification has not proved itself superior. I believe that we should be greatly encouraged and that an insulin similar in some respects to NPH-50 insulin but better in several respects can and should be devised.

Dr. Henry T. Ricketts, Chicago: One of the prime requirements of an intermediate insulin is that it have an effect lasting twenty-four hours, preferably a few hours longer, in all patients. Globin insulin too often fails to meet these requirements. The mixing of regular or crystalline and protamine zinc insulin, when made by patients in the syringe, is technically too difficult for the unintelligent and involves some question of accuracy, not to mention convenience. NP-50 insulin, which closely resembles the 2:1 mixture in its effect on the blood sugar, has proved to be too unstable to justify its being placed on the market. NPH-50 insulin would seem to lack the drawbacks of the other forms and to retain the advantages they have offered. Our experience with it is in substantial agreement with that of Dr. White. We have found, in a series of ambulant patients which did not include children but did include a number of severely diabetic young adults, that this form of insulin controlled glycosuria fully as well as a 2:1 mixture or as NP-50 insulin in 22 of 23 cases. Indeed, it was difficult to see that there was any real difference between any two of these preparations with respect to dosage requirements, time-activity characteristics or the frequency, timing or severity of reactions. In 1 case it was necessary to add 10 units of crystalline to 60 units of NPH-50 insulin to control the blood sugar level after breakfast—a procedure which worked out well. In two other cases, small amounts of supplementary crystalline insulin were given separately, with good results. In addition to meeting the minimum requirement of a full twenty-four hour effect, modified protamine insulin appears thus far to have enough carry-over that the admixture of small amounts of crystalline insulin, necessary in some cases of severe disease to prevent hyperglycemia after breakfast or after lunch, hastens the onset of activity without reducing the duration of activity below twenty-four hours. That is an important feature. It should be stated, however, that not enough data are available to establish this point with certainty.

NPH-50 is still not an ideal insulin, but the day of the ideal insulin is not at hand. Meanwhile, there is little point in continuing a preparation—protamine zinc insulin—which has to be hand mixed with another for the single dose management of persons with severe diabetes, if a more effective manufactured preparation, satisfactory for the vast majority of patients and capable of further modification when necessary, can be made available.

Dr. Priscilla White, Boston: I hope that Dr. MacBryde or others will discover an even better insulin than NPH-50, but I agree with Dr. Ricketts that at the present time it would be desirable for this modified protamine insulin to be put on the market.

THE USE OF ANTIBIOTICS

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Until recently the problem of the proper antibiotics to use in the treatment of infectious diseases was comparatively simple. The physician who was faced with an infectious disease in which antibiotic systemic therapy was indicated administered either penicillin or streptomycin or both, and that was that. During the past year this relatively happy state of affairs has been rudely interrupted by the appearance of aureomycin and chloramphenicol (chloromycetin®), two antibiotics which possess wide and effective ranges of action. The result is that careful attention must now be given to the choice of the antibiotic to be used in the treatment of any individual patient, and in certain instances of disease the problem becomes one of choosing the most effective combination of the several antibiotics.

It will be our purpose in this report to attempt to assess current information concerning the choice of antibiotics, to propose adequate dosage schedules and to discuss the toxic reactions which may occur when these agents are used in the treatment of infectious diseases. It should be obvious that certain of our recommendations will necessarily be tentative, because information concerning the comparative values of aureomycin and chloramphenicol when these are used therapeutically against some infectious diseases is scanty. It should also be borne in mind that, except in those cases in which combined therapy is indicated, no mention will be made of the comparative value of the sulfonamide drugs.

The physician who is confronted with an infectious disease which will respond to several antibiotic agents must consider the following questions in selecting the drug with which to treat the disease:

Which antibiotic will be most effective?

What is the relative toxicity of the agent in the dosage prescribed?

With what ease can the compound be given?

What will the cost of the antibiotic, or the auxiliary costs of its administration, be to the patient?

All are important, but, in these days when the costs of medical care are at a peak, the last two questions should enter into each physician's calculations. If two agents are equally effective against a given infectious process, then the one which will bring about a betterment at the lowest cost to the patient should be used. This does not necessarily mean the cheaper antibiotic but rather the antibiotic which can be given with least auxiliary charges, such as those of hospitalization and frequent visits of patient or physician. Thus a more expensive antibiotic which can be given safely and effectively by mouth in the home might be the choice rather than a cheaper one that requires hospitalization or the physician's frequent attendance for its administration. There are, however, certain exceptions to these generalizations. If a life is at stake, neither the patient nor the physician should count the cost, and every step should be taken which will bring about recovery from the infection.

Tables 1, 2 and 3 present in general terms the antibiotics of choice for the treatment of infections of average severity. As will be noted, when two antibiotics are of equal effectiveness, they are so listed. If the infection is severe, then combinations of equally effective, or primarily and secondarily effective, antibiotics should be used. In our opinion, subacute bacterial endocarditis presents a typical example of an instance in which more than one antibiotic might be given. If the infecting organism is a gram-positive coccus, we believe that an adequate combination of penicillin, streptomycin and aureomycin should be used; if a gram-negative organism is at fault, a proper combination of streptomycin, aureomycin and chloramphenicol should be administered to the patient. In severe influenzal meningitis or in gas gangrene, the use of one of the diazines is always to be recommended as an adjunct to antibiotic therapy. In other infections the diazines may be used in conjunction with the chosen antibiotic agent if in the physician's opinion it will hasten the patient's recovery. It is well for the physician to remember that sulfonamide drugs, penicillin, streptomycin, aureomycin and chloramphenicol all attack and damage different systems in susceptible infecting micro-organisms. The intelligent exploitation of this knowledge will result in prompt and satisfying cures of infectious diseases.

TABLE 1.—*Present Day Usage of Antibiotics in Infections*

Type of Infection or Disease	Penicillin G	Streptomycin	Aureomycin	Chloramphenicol
I. Group A beta hemolytic streptococcic infections	I	III	II	..
II. Alpha hemolytic streptococcic infections	I	II	II	..
III. Streptococcus faecalis infections (group D)	II	..	I	..
IV. Pneumococcic infections	I	III	II	..
V. Meningococcic infections	I	..	U	U
VI. Gonococcic infections	I	II	III	III
VII. Staphylococcic infections				
A. Mild or moderate	I	..	II	..
B. Severe	I*	..	II*	..
VIII. Acute brucellosis	..	..	I	I
IX. Whooping cough	..	?	?	U
X. Tularemia	..	II	I	U
XI. Typhoid	..	..	II	I
XII. Influenzal meningitis				
A. Moderate	..	..	I	U
B. Severe	..	II+S.D.	I+S.D.	U

Key: I indicates first choice; II, second choice; III, third choice. A blank signifies that the drug is of little value. U means that the effect is unknown. S.D. stands for sulfadiazine.

* Combined therapy is used.

In table 4 the dosage schedules of aureomycin and chloramphenicol currently used for children are outlined. Again we must state that these are tentative and will probably be revised as more experience is at hand. It has not been considered necessary to discuss the dosage of penicillin, streptomycin or dihydrostreptomycin with regard to children at this time. Directions concerning the use of these antibiotics are contained in "New and Nonofficial Remedies," [1] to which the physician is referred for such information. Also, it can be said that valuable instructions for using these antibiotics are contained in the package inserts of brands which have been accepted by the Council of Pharmacy and Chemistry of the American Medical Association.

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1. New and Nonofficial Remedies, Philadelphia, J. B. Lippincott Company, 1949.

When aureomycin or chloramphenicol is being used against moderate or severe infections, it is well to start with "priming" doses of the antibiotic of choice. In this way, an effective blood concentration of the antibiotic will be established promptly. As will be noted in table 4, for moderately severe infections the initial dose is divided into three "priming" doses, which are given by mouth at hourly intervals. The total daily maintenance dose is calculated on the basis of the weight of the patient and is divided into six equal parts (or as nearly as is practical); a part (dose) is administered at each four hour interval until the infection is controlled. In patients who are severely ill, and for whose treatment aureomycin has been chosen, the initial "priming" doses may be given by the oral and/or intravenous route. Combined oral and intravenous therapy is generally needed only in instances of the most severe disease. At the time of this writing, preparations of aureomycin suitable for intravenous use have not been approved for commercial distribution by the Food and Drug Administration. It is believed, however, that such dosage forms will be generally available by the end of this year. If the "priming" doses are being given by mouth, the indicated total initial dose of the antibiotic should be divided into three parts and given at hourly intervals, while, if the intravenous route is used, the total "priming" dose should be administered at one time. Then, maintenance doses of aureomycin should be given as outlined in table 4 until the symptoms and signs of the disease are controlled and the temperature has been normal for at least forty-eight hours. (For infants the aureomycin may be dissolved in the formula.) In the treatment of rickettsial infections it is generally safe to withdraw the antibiotic at this point. In the treatment of bacterial and viral infections the dose may be halved at this point and its use continued for five to seven days, except with those patients initially suffering from bacteremia or meningitis. With these the antibiotic should be administered at the higher dosage level until in the physician's opinion the patients are well.

As chloramphenicol may be given only by mouth, the instructions contained in table 4 should be followed, and, as far as the maintenance dose is concerned, the instructions just laid down for aureomycin will suffice. Dosage schedules for adult patients are listed in table 5. If nausea or vomiting appears, it is well to give an adequate amount of an antacid with each dose of the antibiotic. In a certain number of instances this adjunct therapy will relieve the nausea and prevent vomiting. It has been noted that the severe vomiting which may occur when aureomycin is being taken by mouth can frequently be eliminated if a shift to intravenous therapy is made. Finally, it has been noted with certain patients to whom apparently adequate doses of aureomycin have been administered by mouth without achieving the desired effect, a shift to intravenous injection of this antibiotic will bring about a prompt betterment of the patient's condition.

TABLE 2.—*Present Day Usage of Antibiotics in Infections*

Type of Infection or Disease	Penicillin G	Streptomycin	Aureomycin	Chloramphenicol
I. Urinary tract infections				
A. Escherichia coli	..	II	I	I
B. Aerobacter aerogenes	..	II	I	I
C. Proteus vulgaris	..	II	..	I
D. Pseudomonas aeruginosa	..	I	..	II
E. Streptococcus faecalis	II	..	I	..
II. Tuberculosis	..	I	U	U
III. Chancroid	..	I	I	..
IV. Friedländer's bacillus infections	..	I	U	U
V. Salmonella infections (food poisoning)	..	..	?	?
VI. Bacillary dysentery	..	..	U	U
VII. Plague	..	I	U	U
VIII. Subacute bacterial endocarditis				
A. Alpha streptococcus	I	..	II	..
B. Str. faecalis (group D)	I*	I*	I*	..
C. Staphylococcic	I*	..	II*	..
D. Gram-negative bacillary	..	I*	I*	I*
IX. Trachoma	I	U	U	U
X. Surgical conditions of the bowel (preoperative and postoperative)	..	I-SS	U	U
XI. Pulmonary conditions (preoperative and postoperative)	I	I	U	U

Key: I indicates first choice; II, second choice; III, third choice. A blank signifies that the drug is of little value. U means that the effect is unknown. SS stands for succinylsulfathiazole.

* Combined therapy is used.

TABLE 3.—*Present Day Usage of Antibiotics in Infections*

Type of Infection or Disease	Penicillin G	Streptomycin	Aureomycin	Chloramphenicol
I. Rickettsial diseases	..	..	I	I
II. Primary atypical pneumonia	..	..	I	U
III. Psittacosis	II	..	I	U
IV. Lymphogranuloma venereum	II	..	I	U
V. Anthrax	I+S.D.	..	U	U
VI. Syphilis	I	..	II	..
VII. Yaws	I	..	U	U
VIII. Granuloma inguinale	..	I	I	U
IX. Rat bite fever				
A. Spirillum minus	II	..	I	U
B. Streptobacillus moniliformis	..	I	U	U
X. Gas gangrene	I+S.D.	..	U	U
XI. Influenza	..	..	..	..
XII. Common cold	..	..	..	..
XIII. Rheumatic fever (prophylaxis only)	I (or S.D.)	..	..	..

Key: I indicates first choice; II, second choice; III, third choice. A blank signifies that the antibiotic is of little value. U means that the effect is unknown. S.D. stands for sulfadiazine.

TABLE 4.—*Dosage Schedules of Aureomycin and Chloramphenicol for Children*

Severity of Illness	Aureomycin				Chloramphenicol	
	Initial Priming Dose, Mg. per Kg. of Body Weight		Total Daily Maintenance Dose, Mg. per Kg. of Body Weight		Initial Priming Dose, Mg. per Kg. of Body Weight	Total Daily Maintenance Dose, Mg. per Kg. of Body Weight
	Oral*		Oral†		Oral*	Oral†
Moderate	10		25-50		60	30-60
	Oral*	Intravenous‡	Oral†	Intravenous§	Oral	Oral
Severe	20	5	100	15	60	60-120

* The oral priming dose should be split into three parts and given at hourly intervals for three doses.

† The oral maintenance dose should be split into six parts and a part given every four hours.

‡ The intravenous priming dose should be given in one dose.

§ The intravenous maintenance dose should be split into three parts and a part given every eight hours.

TOXIC REACTIONS

The toxic reactions occurring in the course of the action of penicillin or streptomycin are well known and will not be discussed. While dihydrostreptomycin produces a smaller percentage of toxic reactions than does streptomycin, it must be borne in mind that it can

produce the serious reactions which have been noted in the course of streptomycin therapy. To date, and this may change as time elapses, the toxic reactions reported to be produced by aureomycin or chloramphenicol have been nausea, vomiting and looseness of the bowels. In this respect, aureomycin administered by the oral route appears to be a greater offender than chloramphenicol. It would appear reasonable to administer vitamins, in amounts adequate to supply the total daily requirements of the accessory food factors, to patients receiving either aureomycin or chloramphenicol for extended periods. This suggestion is based on the possibility that the disturbance of intestinal function often noted in these patients may produce subclinical vitamin deficiencies. It has also been noted in patients who are receiving aureomycin that an excoriation may occur around the anus as a result of diarrhea. Also, a few patients who receive aureomycin in heavy dosage may show euphoria. It should be said that all of the toxic reactions noted so far in the course of aureomycin or chloramphenicol therapy are more frequent in ambulatory than in bedded patients.

TABLE 5.—*Dosage Schedules of Aureomycin and Chloramphenicol for Adults*

	Aureomycin				Chloramphenicol	
Severity of Illness	Initial Priming Dose, Mg. per Kg. of Body Weight		Total Daily Maintenance Dose, Mg. per Kg. of Body Weight		Initial Priming Dose, Mg. per Kg. of Body Weight	Total Daily Maintenance Dose, Mg. per Kg. of Body Weight
	Oral*		Oral†		Oral*	Oral†
Moderate.....	10		30		60	30-60
	Oral*	Intravenous‡	Oral†	Intravenous§	Oral	Oral
Severe.....	15	5	50-60	15	60	60-120

* The oral priming dose should be split into three parts and given at hourly intervals for three doses.
† The oral maintenance dose should be split into six parts and a part given every four hours.
‡ The intravenous priming dose should be given in one dose.
§ The intravenous maintenance dose should be split into three parts and a part given every eight hours.

CONCLUSION

With multiple antibiotics at his disposal, the physician must choose carefully and wisely from among them, in order that his patient may receive the most effective and economical type of antibiotic therapy.

ABSTRACT OF DISCUSSION

DR. VERNON KNIGHT, New York: An important aspect of therapy in infectious disease, as Dr. Long has mentioned, is that of the simultaneous use of antimicrobial agents. It has been possible in some instances, and in particular against group D streptococci from patients in New York Hospital with subacute bacterial endocarditis, to demonstrate an additive or synergistic effect with penicillin and streptomycin in vitro. Moreover, the combined treatment of these infections with these agents has resulted in an eminently more satisfactory proportion of recoveries than formerly, when these agents were employed singly. As Dr. Long mentioned, one of the most surprising occurrences in the use of chloramphenicol and aureomycin has been their lack of serious toxicity. In an investigation in Mexico in which more than 50 patients with typhoid were treated, oral doses of aureomycin as high as 18 to 24 Gm. daily were administered to adults with no more than moderately severe vomiting or diarrhea as evidences of toxicity. In children doses of 400 to 500 mg. per kilogram of body weight per day were employed without serious toxicity. Chloramphenicol has been administered regularly for several days in doses of 100 mg. per kilogram per day without serious toxicity. Dr. Long has mentioned the intravenous use of aureomycin. It appears to be a practical mode of administration, and my associates and I have used it successfully in the dosages he has recommended in a variety of infections, including murine typhus, peritonitis, puerperal sepsis and staphylococcic infections. After the administration of aureomycin by this route to 10 patients with measles, no consistent pattern of recovery was observed and it was believed that significant beneficial effect had not been exerted. Of particular interest is the use of aureomycin in pertussis. In the past season this drug has been used in the treatment of 6 infants with this disease in a joint project with the U. S. Army Dependents Hospital at Fort Hamilton, N. Y. Oral dosages as high as 333 mg. per kilogram per day were employed for periods up to ten days. Drs. Miller and Ross reported that all these patients displayed improvement within three to four days after initiation of therapy, with disappearance of cyanosis and vomiting, and that by the seventh to tenth day all these patients were no longer whooping and were greatly improved. A favorable report of the use of aureomycin in 20 other patients with pertussis appeared in *Public Health Reports* for May 13, 1949.

DR. ROBERT B. LAWSON, Winston-Salem, N. C.: Dr. Long has stressed the value of combined therapy for serious infections in which there may be bacterial resistance to one agent alone. This important concept suggests that these infections should be hit hard at once with a combination of therapeutic agents rather than using the agents in succession, as is so often done in practice. It is important to bring out, however, that this type of therapy demands a painstaking search for the specific offending organism and in no way justifies "shotgun" treatment without an etiologic diagnosis. A good example is the physician's approach to meningitis: the excellent results of modern treatment for this disease rest on an accurate and early diagnosis of the specific organism made by good laboratory technic. It is only when one has this information that combined therapy can be used intelligently and effectively. Along with the knowledge of what these antibiotics will do, one must keep in mind what they will not do, in order to avoid needless expense to the patient and disappointment to the physician. The vast majority of infections in children are due to virus and other agents that are not affected by the antibiotics rather than to bacteria known to be susceptible. For this reason, the physician must continually keep in mind the need for differentiating those children who require specific treatment and will respond quickly from the larger number who have self-limited virus infections of an ill-defined nature, in whom specific treatment is neither necessary nor successful. I would like to mention the problem that Dr. Long touched on, namely, the appearance of the "serum sickness" type of reaction following the administration of penicillin. This is of particular importance to pediatric groups, because penicillin has frequently been given for pharyngitis; the later appearance of joint pain and swelling has been confusing in the differential diagnosis of rheumatic fever and has caused needless treatment of children for rheumatic fever. What are the comparative blood levels when aureomycin is given in a milk formula to children?

DR. PERRIN H. LONG, Baltimore: In response to Dr. Lawson's question, my associates and I have performed estimations of the concentration of aureomycin in the blood of infants who were not ill and who were getting aureomycin in their formulas. We have not noted any great differences in the concentration of aureomycin in their blood serum from that in little children who received aureomycin in capsules. We believe that it has been an inaccurate procedure, and one which has practically not revealed anything more than whether or not there was aureomycin in the serum. For that reason, I strongly advise the physician prescribing aureomycin not to worry about cluttering up the hospital laboratory with tests for the concentration of aureomycin because, even with the most careful technics it is not yet known how great is the error in these estimates. I do not recommend determining aureomycin blood levels as a routine procedure. I believe that if one sees the patient a couple of times a day and watches his temperature chart and his clinical condition, one knows whether the patient has had enough aureomycin; if his temperature is not down to normal in forty-eight hours and you are treating him for something that you know can be cured by the drug, then give the patient a little more aureomycin.

PHYSICAL MEDICINE IN PERIPHERAL VASCULAR DISEASES

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In a recent book on the diagnosis and treatment of peripheral vascular diseases, an outline classification of diseases and abnormalities of the blood and lymph vessels of the extremities occupies seven and one-half pages.[1] From the point of view of prevalence, by far the great majority of these can be grouped under the headings, "Arteriosclerosis Obliterans," "Thromboangiitis Obliterans," "Raynaud's Syndrome," "Varicose Veins" and "Thrombophlebitis."

DIAGNOSIS

A patient may complain of discomfort or of pain either on exertion or at rest, of coldness in the extremities and of limitation in his ability to walk. Arteriosclerotic changes are most apt to occur in the older person, particularly the one with diabetes. The initial symptoms in thromboangiitis obliterans usually show themselves before the age of 45 and only in men (with rare exceptions). Raynaud's syndrome is observed most frequently in women. Enlargement, inflammation and thrombosis of veins may involve various etiologic factors.

Objective observations include a change in color, particularly on elevation or dependence of the involved extremity, diminished skin temperature and absence of pulsating arteries. The observation of a warm foot, normal in appearance, which does not pale quickly on elevation or become turgid on dependence, with pulsating blood vessels should cause the examiner to seek some other explanation for complaints of pain in the foot and leg. When pulsating blood vessels are present, particularly in the lower extremities, the ability to detect them is enhanced by a proper technic which permits relative relaxation of the examiner's fingers.

Most cases of moderately advanced peripheral vascular disease can be detected by the history and physical criteria as described. In some instances it may be difficult to make a diagnosis without the further aid of some special apparatus. These include the oscillometer, which gives evidence of the gross pulsations of an extremity, and the skin surface thermometer, which conveys more exact knowledge than the examiner's hand. The skin thermometer (usually electric) reveals considerable information concerning the status of the circulation especially when employed in conjunction with the application of heat to a remote extremity. Normally, vasodilation takes place in the lower extremities in response to immersion of the forearms in warm water.[2] This rise will occur usually within fifteen to twenty minutes and to the level of that shown by the skin of the torso and forehead. A slow rise and to a temperature height below this level or a complete absence of rise indicates peripheral vascular abnormality. The mechanism by which hot baths affect the surface temperature of the toes has been studied by Pickering.[3] He showed that the warm blood returning from the upper extremity affected the heat-regulating center in the brain and that secondary nervous impulses to the lower extremities resulted in vasodilatation. Such nervous impulses are carried by the sympathetic nervous system. The removal of the sympathetic vasoconstrictor influence causes an elevation of the temperature of the skin surface of the extremities when vasospasm exists, but not when organic disorder is the cause of the vascular difficulty.[4] Associates and I have shown that the changes noted in the skin surface temperature of the toes following hot forearm baths were not accompanied by corresponding changes in the calf muscles.[5]

Other special technics for the detection of peripheral vascular disease include use of the plethysmograph,[6] arteriograph [7] and phlebograph,[8] capillary studies,[9] production of sweating,[10] production of histamine flares,[11] tracing of radioactive isotopes [12] and use of the ergometer.[13]

TREATMENT

All measures to relieve the subject with peripheral vascular diseases are intended to restore the normal balance between metabolic needs and supply of the tissues. These efforts are made to augment the blood supply by vasodilation and by increasing the collateral circulation except in extreme instances. Such an extreme instance occurs when there is no possibility of influencing blood flow, as in thrombosis of the common iliac arteries. Here the reduction of the metabolism of the structures of the lower extremity can be accomplished by the local application of cold. This measure will cause a diminution of the severe pain of these patients.

Heat.—A simple measure to increase circulation, when this is possible, is the use of heat. Heat also causes an increase in the metabolic needs of the tissues to which it is applied. For these reasons, when heat is applied directly to involved extremities it is administered in small doses. When heat is so applied by means of hot water bags, lamps and high frequency currents there is danger of causing thermal damage to tissues in which there is interference with the blood supply. An increase in pain, or the development of an increase in cyanosis, calls for the cessation of the treatment or a reduction in the quantity of energy used. The difficulty may be due to an increase in local tissue pressures, to increased local metabolism without compensating vascular supply or to direct tissue death, inasmuch as poor circulation cannot remove heat as

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1. Wright, I. S.: Vascular Diseases in General Practice, Chicago, The Yearbook Publishers, Inc., 1948.
2. Gibbon, J. H., Jr., and Landis, E. M.: Vasodilatation in Lower Extremities in Response to Immersing Forearms in Warm Water, J. Clin. Investigation **11**: 1019 (Sept.) 1932.
3. Pickering, G. W.: The Vasomotor Regulation of Heat Loss from the Human Skin in Relation to External Temperature, Heart **16**: 115, 1932.
4. Royle, N. D., and Hunter, J. L.: Symptomatology of Complete Transverse Lesions of Spinal Cord, Australian J. Exper. Biol. & M. Sc. **1**: 57 (June) 1924.
5. Friedlander, M.; Silbert, S., and Bierman, W.: Regulation of Circulation in the Skin and Muscles of the Lower Extremities, Am. J. M. Sc. **199**: 657-668 (May) 1940.
6. Burch, G. E.: New Sensitive Portable Plethysmograph, Am. Heart J. **33**: 48-75, 1947.
7. Kleinsasser, L. J.: Peripheral Arteriography, Surgery **22**: 930-944, 1947.
8. DeBakey, M. E.; Schroeder, G. F., and Ochsner, A.: Significance of Phlebothrombosis, J. A. M. A. **123**: 738 (Nov.) 1943.
9. (*a*) Krogh, A.: The Anatomy and Physiology of Capillaries, ed. 2, New Haven, Conn., Yale University Press, 1929. (*b*) Duryee, A. W., and Wright, I. S.: Studies of Human Capillaries: Present Day Technique for Study of Human Capillaries, Am. J. M. Sc. **185**: 664 (May) 1933.
10. Roth, G. M.: Clinical Test for Sweating, Proc. Staff Meet., Mayo Clin. **10**: 383 (June) 1935.
11. Perlow, S.: The Temperature of the Flare as an Index of Intensity of Histamine Skin Reaction, Am. Heart J. **11**: 605 (May) 1936.
12. Elkin, D. C., and others: Study of Peripheral Vascular Disease with Radioactive Isotopes, Surg., Gynec. & Obst. **87**: 1-8, 1949.
13. Wright, I. S.: Vascular Diseases in Clinical Practice, Chicago, The Year Book Publishers, Inc., 1948.

rapidly as normal circulation. The danger of causing thermal damage is further enhanced if thermal sensation is lost in the treated part. A good instrument for mild and prolonged local heating is the thermostatically controlled foot cradle, the air temperature of which is usually maintained between 88 and 95 F.[14] When more vigorous methods of heating are employed, as with large lamps and diathermy machines, it is safest to apply the heat to some remote part of the body, such as the arm or the torso. Electrically heated sheets and blankets now permit a simple technic for the application of mild and prolonged heat to the entire body.

Activity and Rest.—As with heat, exercise can increase both the circulation and the metabolic needs. In cases in which the local circulation is greatly compromised, as indicated by a discoloration of sudden onset or one that rapidly increases, by the presence of gangrene or ulceration or by severe pain during rest, exercise is contraindicated. According to Wright, the extremities should be held about 3 to 6 inches (0.64 to 1.27 cm.) below the position of the heart, because this is the plane at which to obtain the best blood supply as shown by the filling of the superficial veins—indicated by their slight projection above the skin level.[1]

In the absence of gangrene or extensive ulceration, the patient should be encouraged to walk until pain develops. After a rest, he can resume walking. If the involvement is severe, the Buerger type of exercise can be applied while the patient lies in bed. With the patient lying in the supine position, the extremity is elevated 60 to 90 degrees above the horizontal for the minimum time required to produce ischemia (thirty seconds to three minutes). It is then allowed to hang down over the end of the bed until one minute after the appearance of the reactionary rubor (two to five minutes). The leg is then held in the horizontal position for three to five minutes. This cycle is repeated for one-half hour to one hour three or four times a day.[15]

Sanders devised an apparatus which automatically and continuously rocks the bed through an arc of 60 degrees at a slow, regular rate. Patients soon learn to lie and sleep on this device without experiencing any discomfort. It is particularly valuable for those patients in whom the effort required for the performance of the Buerger exercises is too great. In many patients it relieves pain. It is said to retard the decalcification which occurs during prolonged periods of rest in bed. It may be used either continuously or for intermittent periods during the day, by itself or in conjunction with other measures.[16]

Other Vasodilating Technic.—Histamine and acetyl-beta-methylcholine chloride applied by iontophoresis will cause cutaneous vasodilatation and can therefore be employed for the treatment of peripheral vascular diseases. Both these drugs are useful for the care of indolent ulcers. Acetyl-beta-methylcholine chloride iontophoresis is particularly important in the present limited therapeutic armamentarium for use against scleroderma. It can cause symptomatic improvement. Asbestos paper or gauze soaked with histamine acid phosphate (1:1,000) or acetyl-beta-methylcholine chloride (0.1 to 0.5 per cent) is placed on the region to be treated and is connected by suitable electrodes to the positive pole of a unidirectional source of current. The negative pole is connected to a large dispersive pad placed on the back, or elsewhere on the body. Ointments may be used instead of solutions. Details of technic must be followed carefully in order to avoid burns, which can be exceedingly resistant to healing.[17]

Carbon dioxide baths will also cause vasodilatation. It is claimed that carbon dioxide and oxygen are absorbed by the skin. Benatt has stated that carbon-dioxide-containing baths lead to hyperemia and an increase of the velocity of blood flow of the subcapillary venous plexuses.[18]

Recently, drugs have been introduced which exert adrenolytic and sympatholytic actions. Their vasodilator effects can be readily established by plethysmographic and skin temperature observations. They include tetraethylammonium chloride,[19] dibenamine® (N,N-dibenzyl-beta-chloroethylamine)[20] and priscoline® (2-benzyl-4,5-imidazoline).[21] It has been known for many years that other substances cause vasodilation. These include alcohol[22] and acetylsalicylic acid.[23] Among the peripheral vasoconstrictors are tobacco (to which those suffering from thromboangiitis obliterans are particularly allergic)[24] and caffeine.[23]

Sympathectomy is advocated by some surgeons if a preliminary paravertebral block is followed by evidence of increased cutaneous circulation in the foot.[25] Temperature studies failed to reveal any increased blood flow to the muscles of the leg after sympathetic interruption, even though the circulation in the skin was augmented.[26] Objective proof to the contrary is lacking. From the clinical point of view there exists a difference of opinion. Some consider that it is of value when cutaneous circulation is deficient—particularly in the presence of skin ulcers—but it does not help the intermittent claudication. Others consider it a good procedure for both conditions.

Mechanical apparatus designed to produce an increase in peripheral circulation, such as that for alternating negative and positive pressures[28] and for intermittent venous occlusion,[29] are now but little used.

14. Starr, I., Jr.: Thermoregulated Foot Cradle for Treatment of Peripheral Vascular Disease, Proc. Soc. Exper. Biol. & Med. **29:** 166 (Nov.) 1931.

15. Buerger, L.: The Circulatory Disturbances of the Extremities, Philadelphia, W. B. Saunders Company, 1924.

16. Sanders, C. E.: Cardiovascular and Peripheral Vascular Diseases: Treatment by Motorized Oscillating Bed, J. A. M. A. **106:** 916 (March 14) 1936.

17. Bierman, W.: Physical Medicine in General Practice, ed. 2, New York, Paul B. Hoeber, Inc., 1947. Kovacs, J.; Saylor, L. L., and Wright, I. S.: Pharmacological and Therapeutic Effects of Certain Choline Compounds, Am. Heart J. **11:** 53 (Jan.) 1936.

18. Benatt, A.: Behavior of Skin Capillaries Under the Influence of Carbon Dioxide Baths, Ztschr. f. Klin. Med. **126:** 485, 1934.

19. Lyons, R. H., and others: Effects of Blockade of Autonomic Ganglia in Man with Tetraethylammonium: Preliminary Observations on Its Clinical Application, Am. J. M. Sc. **213:** 315-323, 1947.

20. Nickerson, M., and Goodman, L. S.: Physiological Properties of New Series of Sympatholytic Agents, Federation Proc. **5:** 194, 1946.

21. Grimson, K. S.; Reardon, M. J.; Marzoni, F. H., and Hendrix, J. P.: Effects of Priscol on Peripheral Vascular Diseases, Hypertension and Circulation in Patients, Ann. Surg. **127:** 968-991, 1948.

22. Cook, E. N., and Brown, G. E.: The Vasodilating Effects of Ethyl Alcohol on the Peripheral Arteries, Proc. Staff Meet., Mayo Clin. **7:** 449, 1932.

23. Bierman, W.: The Temperature of the Skin Surface, J. A. M. A. **106:** 1158-1162 (April) 1936.

24. Harkavy, J.; Herbald, S., and Silbert, S.: Tobacco Sensitiveness in Thromboangiitis Obliterans, Proc. Soc. Exper. Biol. & Med. **30:** 104 (Oct.) 1932. Wright, I. S., and Moffat, D.: Effects of Tobacco on Peripheral Vascular System, J. A. M. A. **103:** 318 (Aug.) 1934.

25. White, J. C.: Diagnostic Blocking of Sympathetic Nerves to Extremities with Procaine, J. A. M. A. **94:** 1382 (May) 1930. Morton, J. J., and Scott, W. J. M.: The Measurement of Sympathetic Vasoconstrictor Activity in the Lower Extremities, J. Clin. Investigation **9:** 235 (Oct.) 1930.

26. Friedlander, M.; Silbert, S.; Bierman, W., and Laskey, N.: Differences in Temperatures of Skin and Muscles of the Lower Extremities Following Various Procedures, Proc. Soc. Exper. Biol. & Med. **38:** 150, 1938. Grant, R. T.: Observations on the Blood Circulation in Voluntary Muscle in Man, Clin. Sc. **3:** 157, 1938.

27. Footnote deleted on proof.

28. Herrmann, L. G., and Reid, M. R.: Passive Vascular Exercise Treatment of Obliterative Arterial Diseases of the Extremities, J. Med. **14:** 525 (Dec.) 1933.

29. Collens, W. S., and Wilensky, N. D.: Use of Intermittent Venous Compression in Treatment of Peripheral Vascular Disease, Am. Heart J. **11:** 705 (June) 1936.

Clinically, the whirlpool bath has shown itself to be of value, even though objective evidence of increased circulation has not been observed following its application.[30] We have observed the healing of persistent, indolent ulcers occurring on a thrombophlebitic or arteriosclerotic basis (with or without diabetes) following the use of the whirlpool bath medicated with sulfathiazole and with oxygen. The apparatus required for the production of this bath can be simple and relatively inexpensive.[17]

PROPHYLACTIC MEASURES

As Linton has pointed out, peripheral arteriosclerosis is increasing in frequency because of the advancing age of the general population. He therefore has considered it of importance that "There appears to be definite evidence not only that the extremity derives an immediate benefit from this form of treatment (sympathectomy) but also that it is the best protection that can be given to prevent serious vascular disorders with gangrene in old age. In other words, it appears at present writing that the symptoms and signs of peripheral arteriosclerosis may be reversible if sympathectomy is performed early in the course of the disease and provided the sympathetic neurectomy is sufficiently extensive to prevent regeneration." [31]

Inasmuch as there are undoubtedly many elderly persons with mild symptoms of failing peripheral circulation who would not submit to sympathectomy, it might be worth while to consider other nonsurgical preventive measures. Fundamentally, the problem involves the entire subject of the aging human organism. From this point of view, other considerations, such as dietary ones, may be important—particularly in the presence of a high cholesterol blood level. The elderly person might be advised to avoid use of tobacco and caffeine and encouraged to take a drink of wine or whisky. Exercise could be prescribed within the limits of his cardiovascular possibilities—exercise which would be neither vigorous nor prolonged. Maintenance of body temperature with a minimum of metabolic effort could be accomplished by warm climatic surroundings and by warm clothing when the environment was inclement. At night, the use of mild warmth secured from thermostatically controlled sheets or blankets might well encourage the shift of blood to the peripheral blood vessels and so be of value not only to the elderly person's legs, but also to his joints if they are arthritic, to his blood pressure if it is high, and to his insomnia if it is present.

These prophylactic measures might also be of service to the many persons, not necessarily old, who suffer from what might be called subclinical peripheral vascular disease. These are persons whose hands and feet become cold when their environmental temperature drops, who then feel generally uncomfortable and come to hug the fire.

It has been observed that the application of cold causes a reduction in the temperature not only of the skin but also of the deeper structures.[32] It has also been noted that cold applied to one area of the body (as to the forearm) produces a lowering of temperatures in remote regions (as the skin of the foot).[33] The practical application of this objective evidence is to emphasize that those who are required to work in low temperatures should be warmly clothed all over.

30. Cohen, J.; Martin, G. M., and Wakin, K. G.: Effects of Whirlpool Bath With and Without Agitation on the Circulation in Normal and Diseased Extremities, Arch. Phys. Med. **30**: 212-219 (April) 1949.
31. Linton, R. R.: Peripheral Vascular Diseases, New England J. Med. **240**: 645-654 (April) 1949.
32. Bierman, W.: Conductive Cooling of Living Human Tissue, Proc. Soc. Exper. Biol. & Med. **42**: 518-520, 1939.

CONCLUSION

Physical measures play an important part both in the diagnosis and in the treatment of peripheral vascular diseases. In a large percentage of cases relatively simple procedures, such as those commonly employed in clinical inspection and palpation, prove adequate for diagnosis and uncomplicated devices, such as hot water baths, heating pads, electric blankets, lamps, whirlpool baths, exercise and hygienic measures, are adequate for treatment purposes. Some persons who have peripheral vascular disease require the special disciplines which have been developed for the diagnosis and treatment of this condition. These measures may be of service for the prophylactic care and for the comfort of the elderly person and for the subject who shows subclinical signs of inadequate peripheral circulation.

471 Park Avenue.

33. Bierman, W., and Friedlander, M.: Penetrative Effect of Cold, Arch. Phys. Therapy **21**: 588-592 (Oct.) 1940.

INFECTION OF THE HIP BY BRUCELLA SUIS

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Infection of the human being by Brucella organisms is common in the United States. According to a recent editorial [1] in THE JOURNAL OF THE AMERICAN MEDICAL ASSOCIATION, approximately 4,000 cases of human brucellosis are reported annually to the state departments of health, but it is estimated that the truer figure would run to at least 30,000 to 40,000 actual cases annually. It has been known for years that localization is a characteristic of Brucella infection. Such local lesions have been observed in guinea pigs, especially in those inoculated with Brucella suis, and Huddleson [2] has observed suppurative arthritis, osteomyelitis, spondylitis, meningitis, orchitis and abscesses of the spleen, liver, lymph nodes and other soft tissues. Destructive bone and joint lesions have also been noted in cattle, hogs and horses but are considered relatively rare in man. We propose herein to report a case of Brucella suis infection of the hip joint, diagnosed by clinical and bacteriologic means and successfully treated.

A few words about the history of brucellosis are in order. In the British Army Medical Department's statistical report of 1861, published in 1863, Marston [3] first differentiated Malta fever from the other Mediterranean fevers. The causative organism of Malta fever

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From the Section on Orthopedic Surgery (Dr. Coventry and Dr. Ivins, assistant surgeon); the Division of Medicine (Dr. Nichols) and the Section on Bacteriology (Dr. Weed) of the Mayo Clinic.

1. Current Comment: Brucellosis in the United States, J. A. M. A. **134**: 786 (June 28) 1947.
2. Huddleson, I. F.: Brucellosis in Man and Animals, New York, The Commonwealth Fund, 1943.
3. Marston, J. A.: Report on Fever (Malta), Army M. Dept. Statist. Rep. **3**: 486-521, 1863.

was discovered by Bruce [4] in 1887. He obtained the specific organism at necropsy from the spleens of human patients who had died of Malta fever. In 1897 Bang [5] in Denmark discovered the organism which causes abortive fever in cows, but it was not until 1918 that Evans [6] demonstrated the similarity between the organism of Bang's disease and that of Malta fever. Traum [7] in the United States isolated the organism Br. suis in 1914 from the fetuses expelled prematurely from sows. Bang's disease, Malta fever, undulant fever and brucellosis are considered clinically synonymous, preference in the past several years having been placed on the term brucellosis.

The clinical picture of brucellosis is generally well known. Specific bone and joint complications, however, are less generally observed, partly because of their rarity and partly because of the difficulty in making a diagnosis. As mentioned previously, brucellosis is known to localize in certain of the tissues. A generalized form of polyarthritis was carefully described in 1930 by Hardy and associates.[8] In an article published on a study of Brucella infection in Iowa, they noticed that 32 per cent of 375 patients had arthralgia. Less than 2 per cent, however, had actual inflammation of the joints. A similar study by Swartout [9] in 1937 revealed that of 271 patients observed in Southern California 37 per cent had joint pains. Incidentally, 44 per cent had backache and 39 per cent had pain in the back of the neck. In 1939 Hench and associates,[10] in the "Fifth Rheumatism Review," stressed that one should constantly remember that muscle and joint pains and even frank arthritis may be dominant features of brucellosis. They also stated, as we shall discuss later, that cultures of suppurative lesions are likely to be negative unless the peculiar cultural requirements for Brucella are anticipated.

Goldfain [11] in 1938 attempted to prove relationship between chronic, apparently rheumatoid, arthritis and brucellosis. He studied 50 patients who had rheumatic disease by means of agglutination, opsonocytophagic and cutaneous tests. Thirty-one patients were said to have active brucellosis and 5 were said to have showed acquired immunity. In 1943 Goldfain [12] reported 18 cases of ankylosing spondylitis, of which 5 were attributed to chronic brucellosis on the basis of positive cutaneous, opsonin and agglutination reactions. In 1941 Green and Freyberg [13] questioned Goldfain's observations. They studied 50 patients at the University Hospital, Ann Arbor, Mich. Twenty-five of these patients had typical rheumatoid arthritides. Brucellosis did not exist in any of the first group. In the second group there were 3 certain cases and 6 probable cases of brucellosis. Their conclusions were that brucellosis seldom, if ever, causes chronic nonpurulent inflammation of the joints. In 1937 Hardy [14] stated that in the study of the Iowa cases of brucellosis, arthritis was rare in the milder bovine infections but was rather common in the porcine strains. He stated that one third of the cases in Iowa were of the porcine, or Br. suis, variety. As previously stated, arthralgia was noted in 36 per cent of these. It was a prominent symptom, however, in only 7 per cent. Usually, multiple joints were involved, pain shifting from one joint to the other. The knees, elbows, ankles, shoulder, wrists, fingers and toes were involved in that order, and Hardy did not mention involvement of the hips. Complete subsidence of the arthritic manifestations without a residual was the rule. He stated that eroding suppurative arthritis was encountered occasionally, but only in the spinal and wrist joints in his experience.

Hydrarthrosis as a complication of brucellosis was first reported in 1928 by Baker.[15] He described a case showing all the characteristics of hydrarthrosis, in which the patient suffered from infection by Brucella melitensis. The knees swelled at seven day intervals. The fluid was withdrawn, and microscopic examination disclosed many small gram-negative diplococci on the direct smear. These grew luxuriantly on a beef infusion agar medium of a p_H of 7.4 and proved to be Brucella abortus. In 1936 Sharpe [16] reported a second case of intermittent hydrarthrosis in a patient suffering from undulant fever, though Sharpe did not succeed in culturing Brucella organisms from the synovial fluid, the blood or the urine. The agglutination was positive in a dilution of 1 : 400 to 1 : 500.

In 1948 Steinberg [17] reported a case of localized sacroiliac arthritis in a Doctor of Veterinary Medicine, aged 30 years. Involvement was of the left sacroiliac joint. The patient's agglutination titer was from 1 : 320 to 1 : 1,280. Spink [18] reported a similar case of sacroiliac arthritis due to Brucella infection.

The first proved case of Brucella osteomyelitis was reported by Kulowski and Vinke [19] from the Steindler Clinic in 1932. The patient suffered from suppurative spondylitis, and Brucella organisms were cultured from the lesions. In 1940 Steindler [20] surveyed the literature and found that to 1939, 57 cases of osteomyelitis of the spinal column and intervertebral disks had been reported. To these 57 cases he added 4 more. Osteomyelitis of the long bones has also been recognized. Involvement of the long bones by Brucella organisms is summarized by Lowe and Lipscomb,[21] who reported 2 additional cases of proved Brucella osteomyelitis.

4. Bruce, D.: Note on the Discovery of a Micro-Organism in Malta Fever, Practitioner **39**: 161-170 (Sept.) 1887.

5. Bang, cited by Hardy, Jordan, Borts and Hardy.[8]

6. Evans, A. C.: Further Studies on Bacterium Abortus and Related Bacteria: II. A Comparison of Bacterium Abortus with Bacterium Bronchisepticus and with the Organism Which Causes Malta Fever, J. Infect. Dis. **22**: 580-593, 1918.

7. Traum, J., cited by Huddleson.[3]

8. Hardy, A. V.; Jordan, C. F.; Borts, I. H., and Hardy, G. C.: Undulant Fever, with Special Reference to a Study of Brucella Infection in Iowa, Pub. Health Rep. **45** (pt. 2): 2433-2476 (Oct. 10) 1930.

9. Swartout, H. O.: Undulant Fever in Southern California: Recent Data on the Signs and Symptoms, M. Rec. **145**: 319-321 (April 21) 1937.

10. Hench, P. S.; Bauer, W.; Dawson, M. H.; Hall, F.; Holbrook, W. P., and Key, J. A.: The Problem of Rheumatism and Arthritis: Review of American and English Literature for 1937 (Fifth Rheumatism Review), Ann. Int. Med. **12** (pt. 2): 1005-1104 (Jan.) 1939.

11. Goldfain, E.: Chronic Arthritis and Undulant Fever: Their Interrelationship, J. Oklahoma M. A. **31**: 111-114 (April) 1938.

12. Goldfain, E.: Chronic Brucellosal Type of Ankylosing Spondylitis, J. Lab. & Clin. Med. **28**: 1226-1231 (July) 1943.

13. Green, M. E., and Freyberg, R. H.: The Incidence of Brucellosis in Patients with Rheumatic Disease, Am. J. M. Sc. **201**: 495-504 (April) 1941.

14. Hardy, A. V.: Arthritis in Brucella Melitensis Infections, M. Clin. North America. **21**: 1747-1749 (Nov.) 1937.

15. Baker, B. M., Jr.: Intermittent Hydrarthrosis as a Complication of Malta Fever, Tr. A. Am. Physicians **43**: 285-287, 1928.

16. Sharpe, J. C.: Intermittent Hydrarthrosis Associated with Undulant Fever, Ann. Int. Med. **9**: 1431-1436 (April) 1936.

17. Steinberg, C. L.: Brucellosis as a Cause of Sacroiliac Arthritis, J. A. M. A. **138**: 15-19 (Sept. 4) 1948.

18. Spink, W. W.: Pathogenesis of Human Brucellosis with Respect to Prevention and Treatment, Ann. Int. Med. **29**: 238-258 (Aug.) 1948.

19. Kulowski, J., and Vinke, T. H.: Undulant (Malta) Fever Spondylitis: Report of a Case, Due to Brucella Melitensis, Bovine Variety, Surgically Treated, J. A. M. A. **99**: 1656-1659 (Nov. 12) 1932.

20. Steindler, A.: Orthopedic Complications of Brucellosis, J. Iowa M. Soc. **30**: 256-257 (June) 1940.

21. Lowe, G. H., Jr., and Lipscomb, P. R.: Brucellosis Osteomyelitis: Report of Two Cases in Which Shafts of the Long Bones Were Involved, Surgery **22**: 525-529 (Sept.) 1947.

SEPTIC, MONARTICULAR ARTHRITIS

In 1932 a thesis was published which had been written by Strachan [22] in 1911 and submitted to the University of Glasgow, Scotland. In this thesis was reported 1 case of psoas abscess probably due to caries of the lumbar vertebrae. The patient was suffering from brucellosis. In this same thesis Strachan reported joint effusion in 15.3 per cent of brucellosis cases reviewed and cold abscesses in 1.86 per cent. We find here mentioned for the first time involvement of the hip joint by brucellosis. Strachan reported a case of hip joint disease requiring treatment in bed with extension. He also stated that a Dr. A. Garrow [23] of Steytlerville, Cape Colony, recorded in 1910 a case of undulant fever followed by hip joint disease.

O'Donoghue [24] published in 1933 an exceedingly significant case report of a girl aged 12 years, whom he saw while she was acutely ill and while she was suffering from excruciating pain in the region of the right hip. The agglutination test for Brucella organisms was positive in a dilution of 1:160. Roentgenograms showed slight cloudiness in the right hip joint with probable bulging of the capsule. Radical drainage was done and a large amount of pus was evacuated. Cultures of this pus showed Br. melitensis on the ninth day. Solid bony ankylosis ensued after several months of plaster immobilization. This is the first reported case of septic monarticular arthritis proved by the isolation of the organisms (except for the "suppurative spondylitis" previously reported by Kulowski and Vinke.[19] This is not actually a monarticular arthritis, but disk and vertebral involvement). O'Donoghue went on to state his opinion that in the Middle West septic joint involvement may often be due to Malta fever and that joint infections from this cause are probably commoner than has been suspected, because the differential diagnosis between septic monarticular arthritis of nonspecific origin, tuberculous arthritis and some of the other types might easily be overlooked.

In 1936 the second case in this country of monarticular septic arthritis due to brucellosis was reported by Kulowski.[25] The patient, a man aged 32, was a stock buyer. A painful swelling of the wrist developed three months after onset of constitutional symptoms diagnosed as Malta fever. The agglutination was positive for Br. suis. Surgical drainage was done. There is, however, no report of any cultures of fluid from this joint. One must certainly assume that the infection was due to brucellosis. In 1946 Ramseyer [26] of France reported a case of severe arthritis of the hip due to Bang's disease. Agglutination titers were positive on two occasions, in dilutions of 1:20 and 1:1,280. The roentgenologic appearance of the head of the femur was one of severe destructive arthritis. Material for cultures was not obtained.

One can therefore see that the reports of monarticular arthritis due to brucellosis are rare. The case of O'Donoghue [24] is the only one apparently proved by recovery of the organisms from the joint and cultures of these organisms. From our observations, we feel certain that the incidence of monarticular arthritis due to Brucella infection is much greater than has been suspected and a great deal higher than can be proved. One must first suspect the disease, and then the organisms must be cultured from the joint (or, next best, from the blood or bone marrow) before a definite diagnosis of Brucella arthritis can be made. An agglutination of 1:100 or more is suggestive, but it hardly proves that the arthritis is due to Brucella unless the organisms are recovered, and recovery and growth of the organisms is often difficult.

REPORT OF CASE

An unmarried farmer, aged 22, was admitted to the Mayo Clinic June 22, 1947, complaining of pain of eleven weeks' duration in the right thigh. He stated that on March 10, 1947, fourteen weeks before admission, he had had a gangrenous appendix removed by a surgeon in the locality of his home. On the fourth postoperative day pain had developed in the right groin. The pain lasted only twenty-four hours and then disappeared. On the tenth postoperative day he had a similar twenty-four hour episode of pain. On the thirteenth postoperative day he went home. The incision was still draining, but he felt well. Six weeks after he came home pain again developed in the right groin. He walked on crutches and the pain gradually subsided, though it never left completely. Two weeks before admission he was working in the fields when he felt a sudden severe pain in the right thigh and was taken to his local hospital. It was then noticed that he had a temperature of 99 to 102 F. He had been given penicillin and one of the sulfonamide drugs for two weeks prior to admission.

The past history was noncontributory. There were no diseases of note, nor any previous operations except the appendectomy. Examination at the time of admission revealed localization of his pain to the right thigh and groin. His temperature was 99.6 F. He appeared chronically ill and in pain. Cervical, axillary and inguinal lymph nodes were slightly enlarged. The results of general examination were normal except for the right hip area. Any movement of the hip was extremely painful. There was obvious quadriceps muscle atrophy. The result of abdominal examination was normal. There was tenderness in the upper medial aspect of the right thigh with low grade fever. Hip motions on the right were restricted.

During the patient's stay in the hospital he did not have a temperature of more than 99.6 F., except on one day when it went to 101 F. A summary of his laboratory findings during his course in the hospital showed the urinalyses to be all normal. The concentration of hemoglobin on admission was 13.2 gm. per 100 cc. of blood. Erythrocytes numbered 4,400,000 and 4,700,000 per cubic millimeter of blood on two occasions. On admission leukocytes numbered 8,400 per cubic millimeter of blood. They varied between this figure and 4,800 during his stay. The differential blood cell count the day after admission showed 28 per cent lymphocytes, 5.5 per cent monocytes, 64.5 per cent neutrophils and 2 per cent eosinophils. Twelve days later a repeat differential showed 24 per cent lymphocytes, 16 per cent monocytes, 56 per cent neutrophils and 3.5 per cent eosinophils, with 0.5 per cent basophils. Variations in the sedimentation rate were interesting. The day after admission it was 64 mm. per hour (Westergren). Thirty-three days later, it had fallen to 23 mm., eighty-two days later to 4 mm. and when the patient was last seen on Dec. 8, 1948 it was 2 mm. per hour. The flocculation reaction for syphilis was negative. The Mantoux reaction was 2 plus, using single strength purified protein derivative. Brucella agglutinations were positive on the eighth day after admission at 1:800. They remained positive at 1:800 for approximately five months, when the titer fell to 1:200. One year and five months after the patient was admitted the titer had fallen to 1:80. The agglutinations for typhoid, paratyphoid and proteus X 19 were negative. Blood cultures for Brucella were negative eleven days after admission, three months after admission and six months after admission. Roent-

22. Strachan, P. D.: Bone Abscess Following Undulant Fever, Brit. M. J. **2**: 571 (Sept. 17) 1932.
23. Garrow, A., cited by Strachan.[22]
24. O'Donoghue, A. F.: Septic Arthritis in the Hip Caused by Brucella Melitensis, J. Bone & Joint. Surg. **15**: 506-508 (Jan.) 1933.
25. Kulowski, J.: Undulant (Malta) Fever Osteomyelitis and Arthritis, Surg., Gynec. & Obst. **62**: 759-763 (April) 1936.
26. Ramseyer, M.: Un cas d'arthrite coxo-fémorale grave, dû au bacille abortus Bang, Radiol. clin. **15** (supp.): 109-111, 1946.

genograms of the thorax and spinal column were negative, but roentgenograms of the pelvis and right hip revealed osteoporosis of the head of the femur with evidence of early destructive arthritis (fig. 1). This was reported by the roentgenologist, who interpreted these roentgenograms as indicating probable tuberculosis.

The patient's course in the hospital during this first admission was one of gradual improvement in subjective and objective

Fig. 1.—Appearance of hip at time of admission.

observations. After examination of the patient, the suspicion of Brucella infection of the right hip was raised because of the acute onset of severe pain. This was not compatible with tuberculosis. When the Brucella agglutination was found to be positive, treatment was started. The patient was treated with 1 Gm. of streptomycin and 90 grains (about 6 Gm.) of sulfa-

Fig. 2.—Appearance of hip eleven weeks after admission.

diazine per day for nine days. Streptomycin alone was given for eleven days, and then streptomycin with sulfadiazine was given daily for nine more days.

Thirteen days after admission, the right hip was aspirated with the patient under thiopental sodium anesthesia, the hip joint being entered anteriorly. A clear, glairy, slightly thickened fluid was obtained, which looked like fairly normal joint fluid. Smears of this fluid were negative for acid-fast bacilli. Routine cultures were sterile and cultures for Brucella organisms were later reported negative. Two days later, because of the negative smears and fairly normal appearance of the synovial fluid, it was considered best to inspect the hip joint and take a specimen of the synovium. This was done. The fluid this time appeared cloudier and thicker, and there were possibly 2 fluidounces (about 60 cc.) present. The articular cartilage of the femoral head showed severe early degeneration. Several specimens of the synovial membrane, which appeared pale and boggy, were excised for biopsy. Fluid and tissue were sent out in four separate tubes for routine culture, Brucella culture, inoculation of guinea pigs and histologic examination. After closure of the incision a single spica cast was applied. Histologic sections of the tissue showed nonspecific inflammation. The results of routine bacteriologic examination were normal. Cultures for acid-fast bacilli were negative after eight weeks. Cultures were positive for Br. suis. Nineteen days after the synovial biopsy the hip was again aspirated to determine the nature of the fluid. It was fairly bloody, and cultures of the fluid were negative for tuberculosis, Brucella and routine organisms.

Forty-three days after the original admission the patient was dismissed. The diagnosis of Brucella arthritis had been made, and he had been treated with sulfadiazine and streptomycin. He was in a hip spica and was comfortable; the sedimentation rate had fallen from 64 to 23 mm. per hour. Five weeks later he returned. He was walking on crutches, had no pain and had gained 12 pounds (about 5.4 Kg.). The systemic review was negative. His temperature was 98.6 F. The cast

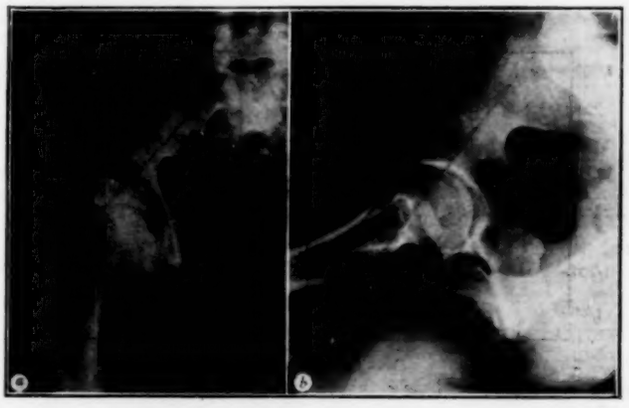

Fig. 3.—Appearance of hip about one and a half years after admission: *a*, anteroposterior view; *b*, lateral view.

was removed, and the hip was found to move without pain. This was in great contrast to his condition at the original admission, when the least motion of his hip caused exquisite pain. Roentgenograms revealed the joint lines in the hip to be quite normal, though some atrophy of bone was still present (fig. 2). The sedimentation rate was normal, now being 4 mm. per hour. Further treatment did not appear to be indicated at this time because of the decided improvement. The patient was allowed to return home on crutches without a cast, but with no weight-bearing on the extremity.

On his third visit, four months after the second, the patient said he had no pain. He had a full range of painless hip motion, except for the last few degrees of internal rotation. Roentgenograms of the hip revealed normal conditions, except for a slight atrophy of bone. He had gained 20 pounds (about 9.1 Kg.) since his original admission; he had no fever, and his sedimentation rate was 2 mm. per hour. At this time we stated that he could start weight bearing.

The fourth admission of this patient was one and a half years after his original admission. He was apparently in excellent health. He had no symptoms whatever. He had been working hard as a farmer since his last dismissal. He did not complain of any pain or stiffness. There was no limp. There was a full range of motion in the left hip except for a few degrees of limitation of internal rotation. Roentgenograms of the hip were negative and looked the same as those of the opposite hip (fig. 3). His agglutination reaction for Brucella

was 1:80 (fig. 4). We considered him cured, although because of the obvious involvement of cartilage at the time of biopsy, a note was made on his record that future hypertrophic arthritis was a strong possibility.

DIAGNOSIS AND BACTERIOLOGY

The diagnosis of brucellosis may frequently be suspected on the basis of history and general clinical observations but can be established with certainty only by bacteriologic procedures. Some investigators attach considerable importance to the opsonocytophagic index, skin testing with brucellergen® or agglutinating a known organism with the patient's serum. However, these procedures have many limitations. The first requires such painstaking laboratory technics and has such limited value that it is seldom available in even the more completely equipped diagnostic laboratories. The skin test is an allergic reaction similar to the tuberculin reaction and depends on the patient's having developed sensitization at some time prior to the test. Also, as with tuberculosis, the duration of sensitization may persist for an indefinite number of years and be falsely interpreted in the course of an acute illness developing later and due to some other agent. Agglutinins commonly develop during the course of the ill-

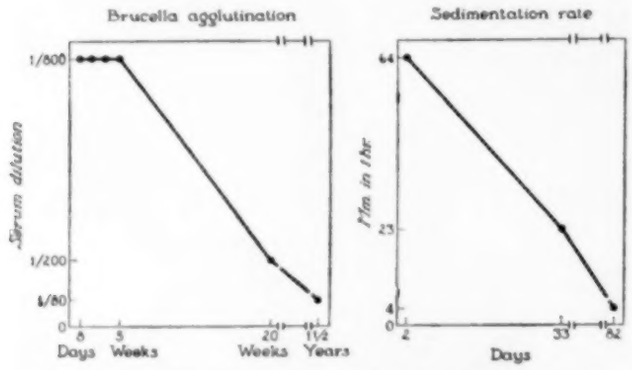

Fig. 4.—Changes in Brucella agglutination and sedimentation rate.

ness, but the rate of development and the final titer vary so that the agglutination reaction may be negative even when the organism has been proved to be present by isolation in pure culture. In some instances it appears that "agglutinin-blocking antibodies" may develop, which will prevent agglutination in the usual manner unless the serum has been heated to 56 C. for fifteen minutes. In other cases the agglutinins may be present in significant titer (1:80 or more) as a result of a previous infection from which the patient has recovered or as a result of his having received either a brucellergen® skin test recently or Brucella vaccine therapy on a so-called therapeutic-test basis. It has recently been shown that members of the military forces who had received cholera vaccine might have significantly high titers of Brucella agglutinins. Serologic information in a given case can therefore have only limited diagnostic value, and conscientious efforts should always be made to isolate the organism.

The isolation of Brucella is usually accomplished by inoculating blood, pleural or abdominal fluid, or urine if uncontaminated with mixed flora, into tryptose broth under 5 to 10 per cent carbon dioxide and incubating at 37 C. In our experience growth will usually begin to appear in two to four days; sometimes six or eight days are required. Some authors have found that cultures required three or four weeks' incubation for primary isolation. Br. abortus usually requires carbon dioxide, at least for primary isolation. Since the gas will not retard the suis and melitensis species, it is well to use it as a routine procedure. If the material is contaminated, as is the case with many biopsy specimens and many urine specimens, the material is best inoculated in quantity on tryptose or meat infusion blood agar plates and incubated in an atmosphere containing carbon dioxide. Animal inoculation (guinea pig) may sometimes be used to advantage, especially if there is much contamination, but it must be recognized that the animals may not show any gross pathologic features at the time of necropsy although the cultures of the spleens may show many colonies of Brucella. Many times the lesions in the liver or spleen may grossly resemble those of tuberculosis. Therefore one must always culture the spleens of the animals and isolate the organism in pure culture or fail to isolate it before making a positive diagnosis of brucellosis or considering it ruled out. It should be emphasized that all tissue, whether a human biopsy or liver, spleen or lymph node from an experimental animal, should be thoroughly minced with sterile scissors, ground to a paste in a sterile mortar and diluted to make a 5 to 20 per cent emulsion which is used for culture. When the medium is inoculated with large pieces of tissue failure to isolate the organism may frequently occur even when it can otherwise be shown to be present.

It will be recalled that the diagnosis in this case was made by isolating the organism from the tissue removed from the hip joint and not from the fluid aspirated from the joint. We have had similar experiences with other patients and with other etiologic agents, and it is our belief that the surgical pathologist must so handle every specimen removed for biopsy that, unless it is of definite neoplastic nature, an ample portion is saved for thorough satisfactory bacteriologic examination. Our experience in human beings and in experimental animals has been that the histologic picture is so variable that one cannot make a positive diagnosis of brucellosis by that procedure alone. It therefore becomes necessary to do extensive bacteriologic studies on the biopsy specimen. This in turn means that the surgeon should obtain as much tissue, pus or fluid as possible and see that adequate portions get to the bacteriologist for thorough bacteriologic study.

TREATMENT

This patient was treated with a combination of streptomycin and sulfadiazine. The results which we have obtained with this method of treatment have been reported in detail elsewhere.[27] That this combination of drugs is a satisfactory method of treating brucellosis has been demonstrated by numerous investigators.[28] In the average case of acute brucellosis with bacteremia we have obtained good results using streptomycin and sulfadiazine simultaneously over a period of twelve to

27. Herrell, W. E., and Nichols, D. R.: The Combined Use of Streptomycin and Sulfadiazine in the Treatment of Brucellosis, M. Clin. North America, **33**: 1079-1088 (July) 1949.

28. Eisele, C. W., and McCullough, N. B.: Combined Streptomycin and Sulfadiazine Treatment in Brucellosis, J. A. M. A. **135**: 1053-1055 (Dec. 20) 1947. Harris, H. J., and Jett, P. C.: Streptomycin and Sulfadiazine (Combined) in Chronic Brucellosis, ibid. **137**: 363-364 (May 22) 1948. Pulaski, E. J., and Amspacher, W. H.: Streptomycin Therapy in Brucellosis, Bull. U. S. Army M. Dept. **7**: 221-225 (Feb.) 1947. Spink, W. W.; Hall, W. H.; Shaffer, J. M., and Braude, A. I.: Human Brucellosis: Its Specific Treatment with a Combination of Streptomycin and Sulfadiazine, J. A. M. A. **136**: 382-387 (Feb. 7) 1948.

fourteen days. In the nonbacteremic forms of the disease in which chronic localized lesions involving the bone or joint have been present, as in this patient, a longer period of treatment has been desirable. Unless toxic effects have been experienced by the patient during administration of streptomycin or sulfadiazine, we have continued administration of the drugs for three to four weeks. The dose of regular streptomycin was usually 1 Gm. each day intramuscularly in divided doses. Neurotoxic effects are seldom encountered when this dose is given. Sulfadiazine was usually administered orally in a dosage of 6 Gm. daily for the same period; in some instances, as in this case, the sulfadiazine was administered in two courses of ten days each with a short rest period between the courses. Inasmuch as this patient has made a complete recovery, it would appear that the drugs used and the plan of administration employed were at least partially responsible for the excellent result obtained.

In general the results obtained from the combined use of streptomycin and sulfadiazine have been satisfactory. However, there have been therapeutic failures and recurrences. Also, the toxic effects often encountered when these drugs are used alone or in combination make this method not entirely desirable for general use. At the present time the combination of aureomycin and dihydrostreptomycin as reported by Heilman [29] and by Herrell and Barber [30] appears to be a more effective method of treating infections due to Brucella and a method associated with a lower incidence of toxic reactions.

SUMMARY

1. A case of septic arthritis of the hip caused by Brucella suis infection has been presented in detail.

2. The diagnosis of Brucella arthritis is extremely difficult because of the problems involved in recovering the organisms.

3. If looked for, the Brucella organisms can be found occasionally in the most unexpected places.

4. In the present case, at least, the organism could be found only in the tissue and not in the synovial fluid.

5. An apparent cure in this case has been effected with the combined use of streptomycin and sulfadiazine.

ABSTRACT OF DISCUSSION

DR. R. BEVERLY RANEY, Durham, N. C.: Advances in chemotherapy have caused great change in the relative importance of various types of pyarthrosis. Acute hematogenous arthritis from staphylococcic or streptococcic infection has declined sharply. Acute gonococcic arthritis is now uncommon. The rarer types of joint infection are therefore assuming increased significance. In this group Brucella arthritis is an important entity. Subclinical brucellosis is a common infection in man; in 1939 Menefee and Poston found that 11.3 per cent of 1,122 Duke University students had positive Brucella agglutinations or positive skin tests. Recent statistics show that 6,073 cases of brucellosis were reported in the United States in 1947. Evans has estimated the actual number of cases to be at least 40,000 a year. Approximately 50 per cent of the patients have joint or muscle pain. Although septic arthritis is uncommon, in about 10 per cent of the cases of brucellosis the joint or muscle pain forms the patient's chief complaint. This may bring him first to the orthopedist. When the patient presents himself with a clinical picture suggesting Brucella arthritis, how can the diagnosis be established? Five immunologic tests are available: agglutination, complement fixation, bactericidal, skin and opsonocytophagic reactions. These tests are not always reliable. To identify a localized infection as brucellosis, the organism itself must be isolated. It has been cultured from joint fluid. Its culture from infected synovial tissue is difficult but, as the reported case demonstrates, can be accomplished. Having made a diagnosis of Brucella arthritis, one is in the fortunate position of being able to give effective antibiotic therapy. Brucella organisms are not affected by penicillin. They are moderately susceptible to sulfonamide compounds and are inhibited by streptomycin. The excellent result obtained by a combination of sulfadiazine and streptomycin in the reported case is evident. The still more effective use of a combination of aureomycin and dihydrostreptomycin recently at the Mayo Clinic has been mentioned.

DR. A. BRUCE GILL, Philadelphia: I am unable to contribute to this excellent paper from personal observations. The number of reported cases of brucellosis has been increasing in this country from 217 new cases in 1927 to 6,073 new cases in 1947. It is most prevalent in Iowa, Illinois, Texas and Wisconsin, although numerous cases have been reported in many other states. Arthralgia and myalgia are present in about one half of the cases, but in only about 10 per cent of the cases do these pains constitute a "chief complaint." In only a small proportion of this 10 per cent are there any objective signs of bone or joint involvement, and permanent joint changes are rare indeed. For this reason the attention of the orthopedic surgeon has seldom been directed toward this disease. There are no pathognomonic clinical signs. The various laboratory tests which the authors have described are difficult and have limited value. A positive blood culture can be obtained in not more than 25 per cent of the cases, and recovery of the organism from synovial fluid is even rarer. The authors have stressed the fact that an absolute diagnosis can sometimes be made only by a bacteriologic examination of affected tissues. The combined use of streptomycin and sulfadiazine has been the most efficacious treatment. It seems probable that aureomycin will eventually replace these drugs in the treatment of brucellosis. We are indebted to the authors for their clear and comprehensive presentation of this subject and for their warning that orthopedic surgeons may at times be called on to recognize and treat this disease.

DR. MARK B. COVENTRY, Rochester, Minn.: I would like to make a plea for biopsy in all cases of monarticular arthritis. Questionable cases should not be assumed to be tuberculous or rheumatic, but every effort should be made to find out what is causing the arthritis. In doing this I believe it is important to remove synovial tissue and inspect the joint. Every effort should be made by the bacteriologist who gets the tissue to examine it for all possible organisms. Even so, we are all disappointed, after obtaining material from the joints, when we find that the pathologist has said "inflammatory" and the bacteriologist has found "no organism," and we are right back where we started. It is my feeling that many of these undiagnosed cases may be due to virus infections and until we can recover the virus organism, culture it, and identify it, there are going to be many cases of monarticular arthritis in which we cannot make a definite diagnosis. I would like to thank Drs. Raney and Gill for their discussion and for their emphasis of the important points in this paper.

29. Heilman, F. R.: The Effect of Combined Treatment with Aureomycin and Dihydrostreptomycin on Brucella Infections in Mice, Proc. Staff Meet., Mayo Clin. **24**: 133-137 (March 16) 1949.

30. Herrell, W. E., and Barber, T. E.: The Combined Use of Aureomycin and Dihydrostreptomycin in the Treatment of Brucellosis, Proc. Staff Meet., Mayo Clin. **24**: 138-145 (March 16) 1949.

Thiamine Deficiency.—Clinical evidence of thiamine deficiency includes polyneuritis (dry beriberi), cardiovascular disturbances and edema. In severe deficiency, acute cardiac failure may occur. Anorexia is common, while neurasthenic symptoms, digestive disturbances and constipation have been reported as early manifestations.—Grace A. Goldsmith, Chemical Measurements in Relation to Physical Evidence of Malnutrition, *Federation Proceedings*, June 1949.

Special Article

CONTROL AND ERADICATION OF BRUCELLOSIS IN ANIMALS

Report No. 1 of the National Research Council, Committee on Public Health Aspects of Brucellosis

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In the United States the policy of attempting to eradicate important livestock diseases has been adopted. The over-all philosophy has been, whenever possible, to live without rather than with many of the diseases which affect domestic animals and especially those transmissible to man. The policy has been economically sound. As a portion of the program, brucellosis of cattle and other domestic animals has received wide attention during the past fifty years. The Committee on Public Health Aspects of Brucellosis was appointed to review the pertinent information about brucellosis and to formulate the report which follows:

From available figures provided by cooperative federal-state records of the control and eradication of bovine brucellosis, approximately 5 per cent of the adult female cattle in the United States are affected with brucellosis. Therefore, at least 1,300,000 dairy and 800,000 beef cows are involved. These 2,100,000 infected cattle are confined to about 20 per cent of the herds throughout the country. From these figures and with the use of prices as of the fall of 1947, it was estimated that the total annual loss from decreased milk production, fewer veal calves and necessary replacements of dairy cows is approximately $92,000,000.

No federal-state figures are available for the incidence of brucellosis in swine, but from packing house surveys it is estimated that between 1 and 3 per cent of the total number are affected.

Brucellosis has proved to be one of the most difficult disease problems. There are many reasons for this, all of which must be understood if the Brucella threat to livestock economy and public health is to be curbed. The livestock disease problems with which we have dealt previously were solved largely by careful study and trial of various control and eradication plans. When the best plan had been developed, it was adhered to until the disease had been controlled successfully. With brucellosis, no single plan has proved effective under all conditions. It has been a real task for some leaders in the eradication of brucellosis to adjust themselves to this situation. The tendency has been to go all out for one particular approach rather than to face the fact that a modification or another plan might be more suitable. The confusion which has existed is to be attributed largely to the different veterinarians' ardent sponsorship of different plans. In most cases a willingness to accept the known information on brucellosis instead of adhering dogmatically to a pet plan would result in less confusion of both the owner and the veterinarian.

One of the difficulties has been the failure to agree on basic procedures and on a nationwide acceptance of them. Instead of getting together on the control and eradication of brucellosis, all have, in too many instances, engaged in the easier method of criticizing one another. Hours have been spent in heated discussion of details which should be left to the persons closest to the work.

A state of emergency has existed for one reason or another during nearly the entire period of fourteen years in which intensive control and eradication of brucellosis have been attempted on a nationwide scale. In the beginning the emergency was cattle surplus. Of late years the emergency has been scarcity. The surplus was related more to poor distribution and lack of purchasing power of the people than to excessive numbers of animals, and the shortage has been the result of demand and not actually fewer animals. During the period of surplus there were more owner demands for help than could be handled, even with the largest number of regularly employed veterinarians in history. As the change from a surplus to a scarcity occurred, the change from a large number of available veterinarians to the most serious personnel shortage experienced in any livestock disease eradication program also occurred. The result of this demand and personnel change has been a decrease of concerted effort. The effort has been spread too thinly. In many cases initial advances have not been followed through. When dealing with infectious diseases, one must continue with sound methods of control and eradication long after the average owner believes that the disease has been eliminated from his herd.

During this period of surplus and scarcity there has been an accelerated traffic in animals. This shifting and intermingling of animals between herds is one of the most serious obstacles to the control and eradication of any infectious disease. With a steady increase in sales barns, truck transportation and even air transportation, this increased traffic in livestock is probably here to stay.

Often there is open conflict between agricultural economics and the public health aspects of brucellosis. Here, again, is further evidence that there must be sound local administration in order to smooth out these differences and establish a workable over-all plan for the area in question.

From the foregoing statements it is obvious that many factors besides scientific knowledge operate in a disease control and eradication program. However, some facts about brucellosis which warrant enumeration have been acquired through observation and research. These are as follows:

1. There is no longer any doubt that a disease of domestic animals caused by members of the genus Brucella is being transmitted to man.

2. No successful practical method of treating brucellosis in animals has been found.

3. The standard serum agglutination test is an efficient but not perfect method of diagnosis.

4. There is no satisfactory practical method of differentiating between the agglutination reaction of the serum of an animal that has been vaccinated with

Brucella abortus strain 19 and that of the serum of an animal infected with fully virulent Brucella organisms.

5. Brucellosis can be eradicated from any herd when the procedures best adapted to the particular herd are followed through under the direction of persons trained in the control of livestock diseases, provided the owner or caretaker of the animals gives his full cooperation. Brucellosis can be eliminated from an area as well as from a single herd.

6. No disease of animals has ever been either controlled or eradicated until the carriers have either been destroyed or restricted in their movement. Failure to recognize this often results in the spread of brucellosis instead of its eradication.

7. To carry out a successful campaign against brucellosis, the cooperation of the producers is absolutely essential.

8. The complex natural course and self-limiting character of the symptoms of brucellosis have resulted in more misinformation than has been encountered with any of the livestock diseases thus far controlled.

9. The nature of brucellosis is such that when an attack occurs the owner usually sustains heavy losses, regardless of any assistance; therefore, the objective should be to locate the infection before its rapid spread occurs. To do this, it is necessary to depend on the best means of diagnosis available at present—the agglutination test. Prevention and not treatment should be the aim.

10. All Brucella-infected females do not abort, but all must be considered potential spreaders of the disease.

11. In order to provide added incentive to initiate disease control and to continue the efforts long after the owner may believe the job has been completed, it has been necessary to spend public funds to aid in defraying some of the expense to the owner.

12. Brucellosis is primarily an animal to animal contact disease. The infected animal is the source of Brucella infection of other animals or of man, either directly or indirectly.

13. Although Brucella abortus commonly infects cows, Brucella suis swine and Brucella melitensis goats, any one of the three types of Brucella may infect all these and other species of domestic animals. This fact requires recognition in control programs.

14. Young animals are less likely to contract permanent brucellosis than older animals. Susceptibility increases with age, up to a point, and the period of the first pregnancy is probably the period of most susceptibility

15. Brucella abortus strain 19 vaccine creates a measure of resistance when injected into cattle. Heifers 4 to 8 months of age usually develop fair resistance but not complete immunity after vaccination. This resistance decreases with time. A few vaccinated young heifers may become permanent reactors. Noninfected heifers and cows of breeding age also develop some resistance after vaccination, but a high percentage of such older animals become permanent reactors after vaccination, as demonstrated by the serum agglutination test.

16. No suitable vaccination has yet been advanced for brucellosis of swine, goats, sheep or horses.

17. Strain 19 vaccine has not been shown to have curative properties.

18. All available evidence supports the view that vaccinating calves with strain 19 does not set up a transmissible animal infection.

19. Vaccination properly falls in the category of an adjunct to control and is not a substitute for other means of control.

20. There are essentialy five fundamental steps which may be used to control and eradicate such an infectious disease:

(*a*) Diagnose the infection.

(*b*) Eradicate the infectious agent.

(*c*) Eliminate the susceptible host (immunization).

(*d*) Maintain the infected animal and the susceptible host apart from each other (isolation).

(*e*) Apply therapeutic measures.

Since no successful practical therapeutic measures are available as yet for brucellosis, the application of some or all of the other four basic steps seems necessary.

21. In view of the worldwide distribution of brucellosis in animals, recognition should be given to the importance of establishing and maintaining adequate restrictions on foreign importations that will minimize the risk of introducing more infection into the country.

With this brief outline concerning various aspects of brucellosis, certain general and specific recommendations may now be made for a nationwide brucellosis control and eradication program. Again it should be understood that many aspects of administration must be left to the local authorities.

BOVINE BRUCELLOSIS

For the control and eradication of bovine brucellosis, this committee believes that the recommendations of the Committee on Brucellosis of the United States Livestock Sanitary Association—the so-called National Plan—should be accepted, and hence the essentials of that report are reproduced here.

Recommendations for National Legislation. — The Secretary of the United States Department of Agriculture should be authorized to promulgate regulations governing interstate movement of animals infected with or exposed to Brucella.

Recommendations for State Legislation.—1. In the intial stages of the control of brucellosis in any area, the state shall sponsor a program when 65 per cent of the livestock owners possessing at least 51 per cent of the cattle have placed their cattle under any one or a combination of the four plans to be set forth in the following pages. Those owners not participating shall not be compelled to come under the program. As control and eradication of brucellosis advance in a given area, the point will eventually be reached where the incidence of infection is very low. At that time the few remaining vestiges or pockets of infection must be eliminated. When 75 per cent or more of the livestock owners possessing 95 per cent or more of the cattle in a given area sign up under any one or a combination of the four plans, the livestock sanitary official

may require the remaining livestock owners individually to select and come under one of the four plans described herein.

2. Reports must be made to the state and federal cooperating agencies, of all activities in connection with the disease, such as vaccinating and testing for agglutinins, on forms furnished by these cooperating agencies.

3. A permanent brand with the letter "B" not less than 2 inches high and 2 inches wide must be placed on the left jaw of every reactor, except registered purebred cattle or cattle eligible to registry otherwise permanently identified. Reactors must also be quarantined to the premises where found, movement of these animals being limited by permit of state officials to slaughter at points where state or federal inspection is maintained, except valuable purebred animals, which must be branded and may be allowed to move on permit of state officials to other herds where Brucella infection is known to exist.

4. All services in connection with the control and eradication of brucellosis should be made available to the owners without expense to them so long as funds are available for such purposes, except the handling of their cattle. When state and/or federal funds are not available, it is recommended that the breeder shall continue his program at his own expense with his private veterinarian under the supervision of state and federal veterinarians.

5. Only vaccine approved and manufactured under license of the Bureau of Animal Industry of the United States Department of Agriculture shall be used in any brucellosis control and eradication program.

6. Authorization shall be provided project workers to enter premises and perform like offices.

7. All phases of official brucellosis control and eradication programs should be conducted under supervision of full time state, federal, county or municipal veterinarians. This provision is not intended to eliminate the practicing veterinarian but is intended to promote and include his services and to provide for supervision of his activities by regularly employed veterinarians.

8. All vaccinated cattle should be permanently identified by tattooing a "V" in the right ear, preceded by the numeral of the quarter of the year and followed by the last number of the year. Thus an animal vaccinated in December 1947 should be marked "4V7." Or they may be hot iron branded on the right jaw, "CV" being used for vaccinated calves and "AV" for vaccinated adults. Special ear tags should also be used in the right ears of all vaccinated animals to aid in recognizing them.

9. A future date should be set after which no female cattle or breeding bulls more than 6 months of age shall be sold and/or moved, except for slaughter, unless such cattle either

(*a*) have been tested for brucellosis and found nonreactive within thirty days prior to the date of sale, or

(*b*) are dairy cattle and breeding cattle less than 24 months of age or feeder cattle less than 30 months of age that were vaccinated against brucellosis with an approved vaccine when they were not less than 6 months nor more than 8 months of age and were identified as provided in paragraph 8 and reported at the time of vaccination to state and federal cooperating agencies, except beef cattle in range or semirange areas, which may be vaccinated at not less than 6 months nor more than 12 months of age, or

(*c*) are in a brucellosis-free accredited herd or area at the time of sale. Accredited herd certificates shall be issued only by the Bureau of Animal Industry, United States Department of Agriculture, and state livestock sanitary officials, under provisions adopted by the United States Livestock Sanitary Association and approved by the Bureau of Animal Industry.

10. Legislation should be broad enough to authorize state livestock sanitary authorities to promulgate, after hearings before representative livestock producers, public health authorities and veterinarians, regulations including the following methods of procedure for eradicating brucellosis:

Plan A: Test-and-slaughter, with or without vaccination of calves. This plan has the advantage of being a short time program, since many lightly infected herds may be freed and remain free from the infection after a limited number of tests. When herds whose serum tests show no agglutination are surrounded by heavy infection, the advantages of calf vaccination should be explained.

Test-and-slaughter is recommended for infected herds in which the immediate removal of reactors will not cause serious economic losses, provided owners follow recognized sanitary procedures, with prompt removal of reactors, thorough cleaning and disinfection of barns or buildings in which reactors have been kept, and retests at intervals not to exceed twenty days until the disease has been eradicated.

The test-and-slaughter plan is likely to be unsuccessful unless all these procedures are followed. However, it has been successful in thousands of herds where suitable precautions have been observed.

Calf vaccination should be encouraged in infected herds and areas but should not be a substitute for sound sanitation and management. Failure to follow sound management practices, so far as replacements are concerned, accounts for most of the breaks in clean herds. Owners should be warned that, as is true in many other disease control and eradication programs, occasional herds do not respond satisfactorily.

Plan B: Test, vaccination of calves and temporary retention of reactors until they can be disposed of for slaughter without excessive loss to the owner under provisions of the law. The objective should be to dispose of reactors for slaughter as soon as possible. Full recognition is given to the fact that vaccinated calves will not all be resistant. However, the percentage of vaccinated animals having increased resistance is sufficiently high to support wider use of this procedure.

Plan C: Calf vaccination without test of any part of the herd. This plan should be confined to those herds in which the movement of animals is restricted to special permits issued by state livestock sanitary officials.

Plan D: Adult vaccination. This should be used only when approval has been received in writing from state and federal cooperating agencies prior to the time of vaccination. It should be confined to herds where there is evidence of rapid spread of virulent infection, indicating the need for emergency measures, and only after the owner has been informed in writing that the vaccinating of his adult animals may not prevent the spread of infection. Herds for which adult vaccination is adopted must be subjected to the agglutination test prior to vaccination, reactors identified as provided for in paragraph 3, and vaccine administered only to brucellosis-free animals within ten days after completion of the official test.

11. Reactors will be classified as under present policies of the United States Bureau of Animal Industry, except

that calves vaccinated at ages from 6 to 8 months, identified as outlined in paragraph 8 and reported at the time of vaccination to state and federal cooperating agencies shall not be classed as reactors until after reaching the age of 2 years. Feeder cattle vaccinated at ages from 6 to 12 months shall not be classed as reactors until after reaching 30 months of age.

Educational Policies.—All properly verified facts concerning the disease and methods of control and eradication should be kept before the public under the direction of persons trained in disseminating information. Such information should include attractively illustrated bulletins and leaflets, based on and confined to present knowledge of the disease which has been properly verified by research and practical application; a moving picture; news releases; radio programs, and all other known methods of publicity.

Frequent group meetings should be held, led by regularly employed state or federal cooperating veterinarians, in the interest of eliminating confusion.

All properly verified useful information which becomes available through research should be disseminated in connection with the control of brucellosis in other animals, including swine, goats and sheep.

SWINE BRUCELLOSIS

Unfortunately, proposals for the control and eradication of brucellosis of swine cannot be substantiated by the vast experience which accompanies proposals for the control of bovine brucellosis. There are no official recommendations, rules or regulations for the control of swine brucellosis that have been tried on a statewide or nationwide basis. In fact, livestock sanitarians and veterinarians have been prone to ignore the effects of swine brucellosis.

In the control of swine brucellosis, it is known that the standard serum agglutination test as now applied is adequate as a herd diagnostic procedure but may not be sufficiently reliable to use in determining the status of the individual animal. Thus, with present methods, the problem of the control and eradication of the disease in swine resolves itself into a herd problem rather than an individual animal problem. This fact alone is highly important, since operations of this nature present innumerable difficulties for any sanitary official when rules and regulations covering the movement and interchange of swine are involved. However, there is some precedent or experience on which to base official rules and regulations governing interstate and other movements of animals when control is conducted on a herd rather than an individual animal basis. Eradication work with such diseases as tick fever, sheep scab, and foot and mouth disease has demonstrated this fact.

Since neither test and immediate slaughter of reactors nor vaccination has been satisfactory in the control of swine brucellosis, the following two plans of control are suggested as a guide for veterinarians and swine raisers:

Plan 1: Sale of entire herd for slaughter. This plan may be applied to herds, large or small, where the primary consideration is the production of pork. It is quick, easy and economical. An interval of three to six months may be necessary to dispose of the entire herd, feeder pigs and all, and to clean and disinfect the premises and equipment. Replacements should be from herds free of brucellosis. Periodic blood tests should be conducted on the new herd as a means of detecting infection that might be present on the premises. Early detection of any swine that may become infected from the premises is essential to protect the entire replacement herd.

Plan 2: Test, segregation and delayed slaughter of infected herd. The details of this plan are:

(*a*) Blood test the entire breeding herd.

(*b*) If infection is present, consider the entire herd as infected rather than remove the positively reacting animals. Manage the herd as a unit.

(*c*) Raise pigs from this infected unit. Wean and test the pigs at 8 weeks of age. Isolate the nonreactors on clean premises as far removed as possible from the infected parent herd. Maintain this isolation until the infected parent herd is disposed of for slaughter.

(*d*) Blood test the pigs up to and during the first pregnancy. Remove all reactors as they occur. Breed to noninfected boars only those gilts whose blood tests are negative.

(*e*) Dispose of the original infected herd as soon as suitable nonreacting replacements are available or as soon as it is obvious that the plan is giving satisfactory results.

(*f*) Thoroughly clean and disinfect premises where an infected herd has been kept, prior to admission of clean replacement stock.

This plan provides for the raising of pigs from the infected parent breeding stock in such a manner that clean replacements of known blood lines are available. The original infected herd must ultimately be disposed of for slaughter, but this is delayed until the quality, the number and the disease status of the pigs are known. This plan avoids the necessity of purchasing replacements from unknown sources and also aids the breeder in maintaining desirable blood lines.

Plan 2 has been used under experimental field conditions and has worked. It is the method of choice for purebred herds or for herds where improved blood lines have been developed even if the ultimate objective of the owner is the production of pork rather than the sale of breeding stock.

The length of time required for disposition of the infected herd will depend on whether the one litter or the two litter system is employed. Naturally the two litter system will involve more difficulties, since numbers of swine alone will tend to complicate control. A decrease of the numbers of breeding swine is advisable in plan 2. In either the one or the two litter system it is necessary that the infected parent swine be completely and permanently segregated from the weaned and tested offspring.

Plan 2 does not necessitate complete cessation of swine production at any time during the operation of the plan, but the chances of success are enhanced if the size of the herd is reduced during the period of segregation.

BRUCELLOSIS IN OTHER ANIMALS

Control and eradication of brucellosis in sheep, goats and horses probably do not require a nationwide uniform program, but cognizance should be taken of the fact that these species may be affected and may transmit the disease to other domestic animals and to man.

SUMMARY

Control of brucellosis in animals is desirable from a strictly agricultural economic viewpoint, but, in addition to that, a public health problem is posed by brucellosis which cannot be measured in dollars and cents. In the light of present knowledge it appears that the satisfactory control and eradication of brucellosis in man are dependent on prevention of the possibility of his being exposed to infected animals and animal products, and thereby are largely a veterinary problem.

Clinical Notes, Suggestions and New Instruments

EFFECT OF DICUMAROL® ON THE ERYTHROCYTE SEDIMENTATION RATE

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The recent common use of dicumarol® in patients requiring the determination of the sedimentation rate of erythrocytes raises the question of how dicumarol® affects the sedimentation rate. The little available information is discordant.

On the one hand, Peters, Guyther and Brambel [1] reported that, with dicumarol® therapy in coronary thrombosis, the sedimentation rate is increased by the drug to such an extent that it no longer serves as an index of healing of the damaged myocardium. Contrariwise, Wright and Prandoni [2] observed that the administration of dicumarol® is not accompanied with an increase in the sedimentation rate. Cosgriff [3] recently reported that the rate is not affected in normal persons. Falk,[4] while stating that the sedimentation rate is affected, expressed the belief that the test has value.

We therefore studied the effect of dicumarol® on the sedimentation rate in the following groups: (1) persons with normal sedimentation rates, (2) patients with myocardial infarction and elevated sedimentation rates who received dicumarol® for therapeutic purposes and (3) other patients with elevated sedimentation rates, but who did not require anticoagulants for therapeutic purposes. We selected patients in this last group with hematocrit readings between 40 and 50 per cent, to avoid the possible effect of anemia on the sedimentation rate.

METHOD AND PROCEDURE

Five cubic centimeters of blood were drawn from the antecubital vein and placed in a test tube containing the Heller-Paul anticoagulant mixture (6 mg. of solid ammonium oxalate and 4 mg. of solid potassium oxalate). The sedimentation rate was measured in Wintrobe tubes. One reading was made at the end of 60 minutes. Prothrombin times were determined according to the Quick method, with Difco thromboplastin. The normal controls ranged between 12 and 14.5 seconds.

Group 1 consisted of 12 persons with normal sedimentation rates, 2 of whom were given one dose of 500 mg. of dicumarol® on the first day of the study only. The other 10 subjects were given daily doses of dicumarol,® the amount depending on the prothrombin time. The daily dosage ranged from 50 to 300 mg. The sedimentation rates were studied daily for seven days. The results showed that, despite the depression of prothrombin to as low as 3 per cent of normal, the sedimentation rates remained normal.

Group 2 consisted of 7 patients with acute myocardial infarction. The effect of dicumarol® on the sedimentation rate in these 7 patients were studied. The drug was given in divided doses, that is, 200 or 300 mg. on the day of admission and then sufficient dicumarol® daily to maintain the blood prothrombin at therapeutic levels (5 to 20 per cent of normal). Dicumarol® did not increase the sedimentation rate. In fact, there was a gradual diminution in the sedimentation rate during the early stage of illness, despite the decreasing levels of the blood prothrombin.

Also included in group 2 were 7 patients selected at random from our case record files, with acute myocardial infarction, treated with dicumarol® and who were admitted in the last two years. The charts were analyzed. It was found that the sedimentation rate followed the clinical course. When the sedimentation rate remained elevated for a prolonged period, sufficient disease to explain this increase was present. Those who were improving clinically showed a decreasing sedimentation rate, despite the fact that the prothrombin levels were either unchanged or even lowered.

Group 3 included 8 patients with medical conditions other than myocardial infarction and with elevated sedimentation rate, but who did not require anticoagulants for therapeutic purposes. Here, too, the sedimentation rate followed the clinical course. The patients who were improving showed a gradual diminution of sedimentation rates, whereas in those whose clinical condition warranted it the sedimentation rate remained elevated. Dicumarol® was given in daily doses to maintain the blood prothrombin at therapeutic levels.

CONCLUSION

Dicumarol® has no effect on the sedimentation rate whether given in therapeutic or somewhat larger doses.

From the Medical and Laboratory Service of the Beth Israel Hospital, New York.

1. Peters, H. R.; Guyther, J. R., and Brambel, C. E.: Dicumarol in Acute Coronary Thrombosis, J. A. M. A. **130**: 398 (Feb. 16) 1946.
2. Wright, I., and Prandoni, A.: The Dicoumarin 3,3'-Methylene-Bis-(4-Hydroxycoumarin): Its Pharmacologic and Therapeutic Action in Man, J. A. M. A. **120**: 1015 (Nov. 28) 1942.
3. Cosgriff, S. W.: The Effect of Heparin and Dicumarol Anticoagulant Therapy upon the Erythrocyte Sedimentation Rate, J. Clin. Investigation **27**: 435 (July) 1948.
4. Falk, O. P. J.: Treatment of Coronary Artery Disease: Dicumarol Therapy, J. A. M. A. **134**: 491 (June 7) 1947.

SEPTICEMIA DUE TO SALMONELLA ENTERITIDIS AND SALMONELLA BLEGDAM

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In August 1947 two of us (M. P. B. and J. H. B.) published a paper entitled "Septicemia due to Salmonella Enteritidis" in the *New England Journal of Medicine*.[1] In a footnote we referred to 14 similar cases which had been observed at an Australian general hospital at Port Moresby, New Guinea, unaware that these cases had been included in a series of 50 cases of infection due to Salmonella enteritidis var. blegdam in Australian soldiers, the details of which were published in the *Medical Journal of Australia* [2] in March, 1946.

On clinical and epidemiologic grounds there was good reason to believe that the patients described in the two papers were infected with the same organism, and efforts were therefore made to compare the strains on which the specific diagnoses had been based. The single strain of Baker and Bragdon,[1] strains from cases 8 and 10 of Fenner and Jackson [2] and N 8 and N 9 of Jones and Fenner [3] were examined by Drs. P. R. Edwards, D. W. Bruner, E. Seligmann and Miss Nancy Atkinson. Dr. F. Kauffman examined the Baker and Bragdon strain. All the strains proved to be S. enteritidis var. blegdam.

We propose herein to correct the mistaken diagnosis of S. enteritidis septicemia.[1] This is of some importance, for there is already considerable confusion in the literature concerning infection due to S. enteritidis associated with invasion of the blood stream.

The strains of Salmonella were examined by Drs. Edwards, Bruner, Seligmann and Kauffman and by Miss Atkinson.

Surgeon (R), United States Public Health Service, National Institutes of Health (Dr. Bragdon); from the Rockefeller Institute for Medical Research, visiting investigator, on a fellowship of the Australian National Health and Medical Research Council (Dr. Fenner) and from the Alfred Hospital, Melbourne, Australia (Dr. Jackson).

1. Baker, M. P., and Bragdon, J. H.: New England J. Med. **237**: 175, 1947.
2. Fenner, F., and Jackson, A. V.: M. J. Australia **1**: 313, 1946.
3. Jones, H. I., and Fenner, F.: M. J. Australia **2**: 356, 1947.

S. enteritidis var. blegdam has been isolated from the blood of human beings in Copenhagen, Denmark,[4] Shanghai, China,[5] New Guinea,[6] Philippine Islands[7] and Louisiana.[8] In 74 of the 80 published cases there was evidence that invasion of the blood stream had occurred. Infection due to S. enteritidis var. blegdam must therefore be considered a severe, widely distributed and not particularly rare disease. In view of the close antigenic resemblance between the two organisms it is possible that other cases of "S. enteritidis" infection characterized by invasion of the blood stream, such as those described by Huang, Chang and Lieu[9] in China and Hayes and Freeman[10] in India, may really have been caused by S. enteritidis var. blegdam.

Council on Physical Medicine and Rehabilitation

REPORTS OF THE COUNCIL

The Council on Physical Medicine and Rehabilitation has authorized publication of the following reports.

HOWARD A. CARTER, *Secretary.*

STEPHENSON RESUSCITATOR, PHYSICIAN'S AND OFFICE MODELS, ACCEPTABLE

Manufacturer: Stephenson Corporation, Red Bank, N. J.

The Stephenson Resuscitator, Physician's Model, is a portable device for delivering oxygen, under alternating positive and negative pressure, to a patient by means of a mask. The weight, complete with tank, is 8 Kg. (17 pounds); the weight when packed for domestic shipment is 9 Kg. (20 pounds), and for foreign shipment 11.4 Kg. (25 pounds). The apparatus is housed in a case with over-all dimensions of 23 by 20 by 48 cm. (9 by 8 by 19 inches). The Council obtained evidence that the device is sturdily built.

It is of the intermittent positive and negative pressure type and can be used as a resuscitator, an inhalator or an aspirator. Positive and negative pressures may be adjusted by using a dial that reads "adult" and "infant" with intermediate gradations. At the "adult" setting a mask pressure of plus 13 and minus 8 mm. of mercury is produced. At the "infant" setting a mask pressure of plus 8 and minus 3 mm. of mercury is produced. These pressures are attained when the resuscitator is held in any position.

When prevented from "cycling" by occlusion of the outlet for negative pressure, the apparatus produced a continuous flow of positive pressure not exceeding 22 mm. of mercury or of negative pressure not exceeding minus 10 mm. of mercury. When a full oxygen cylinder was attached (1,800 pounds per square inch, or 122 atmospheres), it delivered oxygen for twenty-four minutes.

The resuscitator is equipped to deliver pure oxygen or a mixture of air and oxygen. Mixture with air is regulated by a setting on the "face piece" to which the mask is attached. Since a constant flow of oxygen is delivered, depending on the pressure which has been selected, the speed of cycling is regulated by the mixture of air with the oxygen. At the "adult" pressure setting, pure oxygen is delivered at the cycling speed setting of "slow." With the pressure setting at "adult" and the cycling speed setting at "fast," the same volume of oxygen is delivered, but an additional 1.6 volumes of air is delivered. In these circumstances the apparatus cycled 2.6 times as fast. The concentration of oxygen then was about 40 per cent, including the volume of oxygen delivered from the tank and the partial pressure of oxygen in air. Concentrations of oxygen between 40 and 100 per cent were obtainable by altering the setting of the cycling speed regulator between "fast" and "slow."

The apparatus may be used as an inhalator. With the resuscitator attachments being used, the mask is held a small distance away from the face. Failure to attain an appreciable positive pressure in the mask prevents cycling.

A satisfactory aspirator is included, which works by a Venturi effect. The aspirator can be used simultaneously with the resuscitator or inhalator, which may be advantageous in some circumstances.

Stephenson Resuscitator, Physician's and Office Models

A slightly different form of the Physician's Model is called the Office Version. While both types are portable, the Physician's Model is better suited to transportation by automobile in emergencies outside the office, while the stability of the Office Version makes it more convenient for use inside the office. It employs the essential parts already described and in addition a substantial base holding a size D or E oxygen cylinder with the mechanism and a handle affixed to the top. These cylinders are 122 cm. (48 inches) high. Size D has a diameter of 19 cm. (7½ inches), while size E has a diameter of 18 cm. (7 inches).

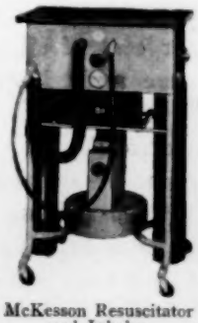
The Council on Physical Medicine and Rehabilitation voted to include the Stephenson Resuscitator, Physician's Model and Office Model, in its list of accepted devices.

McKESSON RESUSCITATOR AND INHALER ACCEPTABLE

Manufacturer: McKesson Appliance Company, 2226 Ashland Avenue, Toledo 10, Ohio.

The McKesson Resuscitator and Inhaler is designed to administer oxygen to apneic patients. The oxygen is supplied either by intermittent positive pressure or by continuous flow at low pressure. Three models are furnished: a portable model in a carrying case and two hospital models, one of which accommodates the small D or E size cylinders and the other two large cylinders. Aspirators and adjustable volume controls are optional on all models.

Accessories include an infant inhaler hood, two other hoods, a head harness, a metal airway (infant size), a metal airway (adult size) and two wrenches. The over-all dimensions of the apparatus are 86 (height) by 46 by 60 cm. (34 by 18 by 22 inches) and the weight is 28 Kg. (62 pounds). The shipping weight is 37 Kg. (82 pounds).



McKesson Resuscitator and Inhaler

Evidence of satisfactory construction and effective operation was obtained from the field and from a laboratory acceptable to the Council. In the announcement of acceptance, however, it is desirable to call attention to certain reservations made in connection with similar apparatus accepted in the past. Possession of mechanical devices for use in resuscitations does not obviate the need of teaching manual procedures, like the Schafer prone pressure method, that are instantly available in emergencies while apparatus is being sought by assistants. This apparatus should be used only by specially trained personnel. With these reservations, the Council on Physical Medicine and Rehabilitation voted to include the McKesson Resuscitator and Inhaler in its list of accepted devices.

4. Kauffmann, F.: Ztschr. f. Hyg. u. Infektionskr. **117**: 431, 1935.
5. Fournier, J.: Bull. Soc. path. exot. **32**: 643, 1939; cited by Kauffmann, F.: Die Bakteriologie der Salmonella-Gruppe, Kopenhagen, 1941, p. 264. Raynal, M. J. H.: Bull. Soc. path. exot. **40**: 212, 1947.
6. Baker and Bragdon.[1] Fenner and Jackson.[2] Jones and Fenner.[3]
7. Stevens, R. B.: J. Bact. **52**: 146, 1946.
8. Holt, R. A., and Newton, H.: J. Lab. & Clin. Med. **33**: 1155, 1948.
9. Huang, C. H.; Chang, H. C., and Lieu, V. T.: Chinese M. J. **52**: 345, 1937.
10. Hayes, W., and Freeman, J. F.: Indian J. M. Research **33**: 177, 1945.

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SATURDAY, OCTOBER 1, 1949

WORLD ASPECTS OF SOCIAL MEDICINE

While the United States is at this time a seething cauldron of discussion relative to social changes in the administration of medical service, the subject is of equal, if not greater, concern in Great Britain and attracts constant consideration in most other countries.

During the war Nazi Germany saw the National Socialist State medicine become an instrument of fascist domestic and foreign policy. According to Rosen,[1] physicians had to accept and further the principles of National Socialism. Research was directed toward justifying National Socialistic racial doctrines. Many health insurance institutions were suppressed. Nature healing was officially recognized. In the ensuing years medicine in Germany deteriorated, became detached from scientific progress and lost such leadership as it had previously had in medical science of the world.

A survey of medical education in Western Germany during 1948[2] calls attention to the fact that purges of faculty members by the Nazi and later by denazification boards and the Allies have seriously depleted the ranks of competent teachers. Nevertheless, the attractions of a medical career are so great that nearly 50 per cent of all higher students in Germany in 1948 were medical students.

Conditions in China have been deplorable for many years. Dr. R. V. Hemenway[3] reports that there has been only one scientifically trained physician for every 156,000 persons in China and that there are fewer hospital beds for all of China than for New York City alone. Scientific medical care for the blind, the crippled, the lepers, the aged and the destitute is totally lacking. At present some progress is being made, but in the midst of civil war, as might be expected, medical institutions suffer.

From Budapest comes a report by Sabanov[4] on thirty years of Soviet public health. He reports 750,000 hospital beds in Russia in 1946, 72 medical faculties with 100,000 undergraduate students and 12 institutes for postgraduate medical study. He reports also that one half of the women from the villages are cared for during childbirth in maternity homes. During World War I, typhus, plague and cholera menaced all Russia. Sabanov says that plague, cholera, smallpox and typhoid have disappeared and that typhus is rare.

A Bulgarian physician, Vassilev,[5] offers a consideration of the present state of medical organization in Bulgaria. His recommendations are significant of what occurs to medical organizations when the state takes over. The abstract indicates that there are in Bulgaria two organizations, one the Bulgarian Medical Association and the other the Union of Public Health Personnel. Vassilev says that the existence of two such organizations is purposeless, since the union has much broader activities. Practically all physicians are employed by the state, and their interests as employees are safeguarded by the union. With the decline of private practice as socialized medicine advances, according to Vassilev, the safeguarding of the interests of private practice becomes practically useless. The union includes all public health personnel, whereas the medical association is limited to physicians, and, according to Vassilev, the union can therefore care much more adequately for productivity in the field of public health. Finally he says, "The Union is more effective and practical in carrying out Marx-Lenin education than the Medical Association."

From Czechoslovakia comes a statement by Málek[6] contrasting existing situations with those that prevailed formerly. He says briefly that the bourgeois-capitalist system in Czechoslovakia gave neither sufficient material nor spiritual incentive to research workers; they were not selected properly, nor were the biologic sciences sufficiently organized. He recommends, therefore, that all these factors be changed. University professors and teachers will be organized not only for research but also to teach and will be held responsible for producing young research workers. Appointments will be for three to five years only, and this, he feels, will give incentive to professors and chiefs to work harder. Finally he suggests, "New scientific societies and institutions will have to be founded in the new socialist society on the pattern of the Viam Institute of the U. S. S. R. or the Rockefeller Institute in the U. S. A." The communist government in Czechoslovakia abolished the medical society within eight

1. Rosen, G.: Medicine under Hitler, Bull. New York Acad. Med. **25**: 125, 1949.
2. Ghent, E. R.: Medical Education in Western Germany, McGill M. J. **17**: 434, 1948.
3. Hemenway, R. V.: Chinese Medicine, M. Woman's J. **55**: 54, 1948.
4. Sabanov, A.: Thirty Years of Soviet Public Health, Népegészségügy **30**: 133, 1949.
5. Vassilev, V.: Professional Unity of Public Health Personnel, Ann. méd. **40**: 790, 1948.
6. Málek, I.: Education of Young Research Workers in Biological Sciences, Časop. lék. česk. **87**: 611, 1948.

months after it took control of the government. It intimated that medical affairs would hereafter be handled through trade unions.

Most of the information here supplied is taken from abstracts which appear in *Excerpta Medica* (Medical Microbiology and Hygiene, July 1949, vol. 2, sect. 4). The abstracts are unusual in that such material does not appear elsewhere and certainly not in easily available abstract services. The material comes from periodicals published in German, Czechoslovakian, Russian, Bulgarian and English languages. Material on other phases of epidemiology is included and actually covers all the important medical periodicals of the world. Nowadays the doctor is not well informed unless he is at least aware of world medical problems.

MATERNAL MORTALITY RATES AGAIN LOWER

Provisional figures on maternal mortality in the United States collected by correspondence with state public health agencies indicate a continuation of the downward trend in maternal mortality rates reported in THE JOURNAL last May. The United States will undoubtedly show a rate of not more than 1.2 maternal deaths per thousand live births in 1948; a drop of 0.1 from the previous year.

Maternal Mortality, 1933, 1947 and 1948
(Deaths per Thousand Live Births)

State	1933	1947	1948	State	1933	1947	1948
Alabama	7.5	2.6	2.3	Nebraska	4.6	1.1	0.6
Arizona	6.5	1.8	1.5	Nevada	8.1	1.2	1.6
Arkansas	7.8	1.8	2.1	New Hampshire	6.9	1.1	1.2
California	4.6	1.0	0.9	New Jersey	5.4	1.0	0.8
Colorado	6.2	1.3	1.1	New Mexico	8.6	2.1	2.3
Connecticut	5.0	0.7	0.6	New York	6.2	1.0	0.9
Delaware	6.9	0.8	0.9	North Carolina	6.8	1.7	1.9
Dist. of Columbia	5.0	1.1	0.7	North Dakota	4.9	1.1	1.1
Florida	11.5	2.2	1.9	Ohio	6.1	1.2	0.9
Georgia	7.5	2.5	2.3	Oklahoma	6.5	1.7	1.2
Idaho	4.3	1.0	0.7	Oregon	5.5	0.9	0.4
Illinois	5.0	1.0	0.8	Pennsylvania	5.8	1.3	0.7
Indiana	5.9	1.1	1.0	Rhode Island	5.7	0.9	0.9*
Iowa	5.3	0.9	0.7	South Carolina	8.0	2.6	2.3
Kansas	5.5	1.0	0.9	South Dakota	4.8	1.0	0.7
Kentucky	5.3	1.8	1.5	Tennessee	6.0	1.7	1.8
Louisiana	8.4	1.9	1.6	Texas	7.7	1.5	1.6
Maine	7.0	1.5	0.7	Utah	4.5	0.8	0.6
Maryland	5.0	1.0	0.9	Vermont	5.7	1.2	1.0
Massachusetts	6.7	0.9	0.7	Virginia	6.3	1.7	1.4
Michigan	6.1	1.1	0.8	Washington	6.4	1.1	0.7
Minnesota	4.4	0.6	0.7	West Virginia	5.7	1.6	1.2
Mississippi	7.3	2.6	2.7	Wisconsin	5.0	1.1	1.0
Missouri	5.8	1.4	1.0	Wyoming	5.7	0.8	1.1
Montana	5.7	1.1	0.9	United States	6.2	1.3	1.2

* 1947 data.

Sources: Vital Statistic Rates in the United States, 1900-1940, United States Department of Commerce, 1940. Maternal Mortality Rates by States, 1947, Federal Security Agency, United States Public Health Service, National Office of Vital Statistics, Release (not dated). Unpublished provisional reports for 1948 from state health departments.

The provisional maternal mortality rates by states are shown in the accompanying table. Twenty-seven states and the District of Columbia have rates at least as low as 1 maternal death per thousand live births. The best state record was the phenomenal rate of 0.4 reported for Oregon. While this rate is provisional, Oregon made an outstanding record in 1948. Three states—Connecticut, Nebraska and Utah—now hold second place, each with a rate of 0.6.

Minnesota had the lowest rate, 0.6, in 1947. The highest rate in 1948 was 2.7, for Mississippi. In 1947, the highest rate, 2.6, was reported for Mississippi, Alabama and South Carolina; the rate for the latter two states declined to 2.3 in 1948. Considering the differences in climate and racial composition, some students of vital statistics may consider the drop from 2.6 to 2.3 for Alabama and South Carolina an accomplishment as great as or greater, from the social point of view, than the reduction for Oregon from 0.9 in 1947 to 0.4 in 1948.

For thirty-seven states and the District of Columbia, the 1948 rates were at least as low as those reported in 1947; the decrease ranged from 0.1 to 0.8. In only eleven states were the rates higher in 1948, and the increases were small—0.1 to 0.4. The progress against maternal mortality in the United States continues to be general throughout the entire country.

Many other nations are also experiencing a considerable drop in their maternal mortality rates. Recently available figures indicate that New Zealand (whites only) experienced only 1.1 maternal deaths per thousand live births in 1947.[1] Probably a number of the European countries that have had outstanding health records in the past also have rates close to this. Obviously future decreases in the number of maternal deaths per thousand live births will be smaller. There are enough states in the United States with maternal mortality rates above 1.0, however, to anticipate some further decreases in the rates for individual states

The spread between the rates of the healthier countries continued to narrow.[2] As maternal mortality rates approach the level of 1.0, they will no longer be a gage for comparison of the health of nations. In fact, a spread of only 0.1 or 0.2 between the rates for any two nations may well be statistically insignificant; that is, the small differences may be due to errors in reporting the number of maternal deaths and live births.

Since 1933, the United States has made tremendous progress, with the rate declining from 6.2 to 1.2 in fifteen years; in 1947 the rates for whites and nonwhites were 4.5 (5.6-1.1) and 6.4 (9.7-3.3) lower than in 1933. The spread between the highest and lowest state rates decreased from 7.2 (11.5-4.3) in 1933 to 2.3

1. The official vital statistics reports for New Zealand feature the maternal mortality rate for whites; rarely is the rate for nonwhites given. The 1947 United States rates were 1.1 for whites only and 1.3 for all races; the nonwhite rate in 1947 was 3.3. The nonwhite rates for New Zealand do not appear in the most recent edition of the "New Zealand Official Year Book." If the over-all rate for New Zealand was actually lower in 1947 than for the United States, the difference could be attributed to a smaller proportion of nonwhites in New Zealand.

2. Sweden, for example, was 3.1 below the United States rate in 1933 despite the fact that less than one fifth of the births were attended by physicians. Since the United States rate for 1948 was 1.2, the 1948 rate for Sweden, which is not now available, could not be more than 1.2 under the United States rate.

(2.7-0.4) in 1948. More important than the decline for the whole nation is the fact that the highest state rate in 1948 was 2.7, which was less than two thirds of the rate, 4.3, for the best state in 1933. To the extent that this one vital statistic can be considered an index of health, the charge that rapid improvement in health has been limited to the wealthier sections of the country is clearly and emphatically refuted.

Current Comment

AMERICAN MEDICAL ASSOCIATION'S STORY IN *LOOK* MAGAZINE

The story of the American Medical Association in the October 11 issue of *Look* magazine will reach millions of readers. The article offers a concise, instructive presentation of the work of the Association and of its program and achievements. A better understanding of American medicine and of what can be obtained under independent and nonpolitical medical effort will be had by those who read *Look's* story.

ESTROGENS AND CANCER

Numerous experiments have shown that estrogens exert a blastogenic effect in various species. Estrogens play an essential role in the development of cancer of the breast in male and female mice of cancer-susceptible strains. A similar response can be elicited in rats subjected to prolonged treatment with estrogens. In guinea pigs myofibroma of the uterus develops following estrogen medication. Administration of estrogens elicits leukemia and tumors of the testis in mice. However, the cancerigenic action of estrogens in man is still controversial although these drugs have been used extensively in medical practice. The normally high frequency of cancer of the breast in women makes difficult the determination of the relation between the development of mammary cancer in women and preceding treatment with estrogens. On the other hand, "spontaneous" cancer of the breast in men is relatively uncommon and its occurrence following prolonged and intensive contact with estrogens would be of definite significance. The fundamental conditions for the observation of such sequelae were created with the introduction of estrogen therapy for the control of cancer of the prostate. It is noteworthy, therefore, that during the last few years there has been a steadily increasing number of reports of the appearance of unilateral or bilateral cancer of the breast in male subjects who received large doses of estrogens over many months.[1] While the total number of instances so far published is not large, the appearance of such cancers has aroused the attention of investigators in this country and in Europe. Recent preliminary observations of male pharmaceutical workers engaged in the manufacture of estrogens provide additional evidence of a relation between estrogenic exposure and cancer of the breast.[2] In this country and abroad hyperplasia of the breasts has developed in male estrogen manufacturers, which creates an increased liability to subsequent cancerous reactions in these tissues. Although the evidence presently available may not be conclusive, it is sufficient to warrant caution in the medicinal and cosmetic use of estrogens, especially if these drugs are employed over long periods of time and in systemically effective doses.

1. Auchincloss, H., and Haagensen, C. D.: Cancer of the Breast Possibly Induced by Estrogenic Substance, J. A. M. A. **114**: 1517-1523 (April 20) 1940.

2. Fitzsimons, M. P.: Gynaecomastia in Stilboestrol Workers, Brit. J. Indust. Med. **1**: 235 (Oct.) 1944. Scarff, R. W., and Smith, C. P.: Proliferative and Other Lesions of Male Breast; Notes on 2 Cases of Proliferative Mastitis in Stilboestrol Workers, Brit. J. Surg. **29**: 393 (April) 1942.

BRUCELLOSIS

In this issue of THE JOURNAL (page 326) appears a report of the National Research Council on brucellosis. Since the condition comes to human beings through contact with infected animals, the public health problem has been the elimination of the disease from animals. The commission which considered the subject is convinced that the disease could not be controlled or eradicated until the carriers among animals were destroyed or restricted in their movements; thus far this has not been possible. A successful method of treatment for animals has not been developed. Apparently aureomycin is efficient in controlling brucellosis in human beings and may well be considered specific for that disease. A method of vaccination has not yet been developed against the occurrence of brucellosis in swine, goats, sheep or horses. The commission feels that five fundamental steps are required to control and eradicate the disease, including diagnosis of the infection, eradication of the infectious agent, elimination of the susceptible host by immunization, isolation of infected animals and the use of therapeutic measures. The costs of treatment of animals with aureomycin would be prohibitive, but the time may come when such methods of treatment may be available to veterinary physicians as they are to physicians who care for human beings. Many will remember that when penicillin was first introduced the costs were tremendous, but still these costs were not considered prohibitive in saving the life of a prize steer with pneumonia. The report of the commission of the National Research Council is a basic document which deserves consideration not only by all especially interested in the field but particularly by legislative bodies concerned with developing legislation to make the attack on the disease effective.

ORGANIZATION SECTION

Official Notes

ESTABLISH GEORGE MINOT LECTURESHIP

For years, officers of the Section on Experimental Medicine and Therapeutics have desired to honor, by establishing a "name lecture," an American investigator who has made an exceptional contribution to the development of clinical investigation and therapeutics. At the Interim Session of the Association in St. Louis last November, three officers of the section, Dwight L. Wilbur, San Francisco; Edgar van Nuys Allen, Rochester, Minn., and Carl V. Moore, St. Louis, suggested that immediate steps be taken to obtain approval of the idea from the Council on Scientific Assembly and that the lecture be named in honor of Dr. George Richard Minot, Boston, whose contributions to medical knowledge of the causes and methods of control of pernicious anemia have been recognized throughout the world. Both suggestions were unanimously supported by the executive committee of the section, and approval has been obtained from the Council on Scientific Assembly. A committe of former chairmen of the section—Drs. Allen, Walter Bauer, Boston, and Carl Dragstedt, Chicago—has been appointed to work out details. The first lecture will be given either at the 1950 or at the 1951 meeting.

Washington Letter

(From a Special Correspondent)

Sept. 26, 1949.

Pay Raises for Veterans Administration Doctors

Proceeding with almost unprecedented speed, the Senate Labor and Public Welfare Committee on September 21 approved a bill that provided for substantial salary increases to physicians, dentists and nurses in the Department of Medicine and Surgery, Veterans Administration. Action was taken only a few hours after a public hearing on the measure (HR 6022) had been held by the subcommittee on veterans legislation, of which Senator Claude Pepper is chairman. HR 6022 was passed by the House in August, and final enactment before adjournment of Congress now appears probable. Testimony in support was presented at the brief hearing by spokesmen for the Veterans Administration and the American Legion.

Philadelphia Teaching Hospitals Join Army in Novel Plan

The so-called Ravdin Plan, by which residents are utilized to relieve shortages of specialists at Army stations, has worked out so well in its first month of trial (September) that it may be extended soon, according to the Surgeon General's Office. Sponsor of the system is Dr. I. S. Ravdin, of University of Pennsylvania Hospital. Cooperating in the plan are heads of major departments at the teaching hospitals affiliated with Jefferson, Temple and Pennsylvania medical schools. Residents who volunteer are assigned for two months' duty at Army posts. The plan has received approval of the several American specialty boards involved to date. First Army stations to get the residents were Camp Knox and Camp Campbell in Kentucky.

U. S. Delegates Attend Radiation Conference

Appointment of eleven radiologists and physicists to represent this country at a three nation conference on radiation tolerances was announced by the Atomic Energy Commission a few days prior to the session, scheduled for September 29-30 at Chalk River, Ontario, Canada. The conference was planned under provisions of the Technical Cooperation Program of the United States, the United Kingdom and Canada, which does not include information on weapons. Establishment of uniform radiation tolerance standards was one of the main objectives.

United States delegates are: Dr. Shields Warren, director, and Dr. John Z. Bowers, deputy director, of the Atomic Energy Commission's Division of Biology and Medicine; Dr. G. Failla, professor of radiology at Columbia University, and Drs. Austin M. Brues, J. G. Hamilton, Louis Hempelmann, Wright Langham, Karl Z. Morgan, Herbert M. Parker, Lauriston S. Taylor and Bernard S. Wolf.

Agenda for Pan-American Meeting

Dr. Fred L. Soper, director of the Pan-American Sanitary Bureau, has disclosed the tentative agenda for the meeting of the Directing Council to be held in Lima, Peru, October 6-12. United States representatives at the meeting will include Dr. Thomas Parran, dean of the newly organized school of public health at the University of Pittsburgh; Dr. Leonard A. Scheele, Surgeon General of the U. S. Public Health Service, and Dr. H. VanZile Hyde, member of the World Health Organization executive board.

Matters to come before the meeting include the Pan-American Sanitary Bureau budget and program for 1950, plans for construction of a headquarters building in Washington, annual observance of Pan-American Health Day, arrangements for a number of inter-American medical congresses and elections to three vacancies on the executive committee.

Hospital Managers' Training Institute

The Veterans Administration will conduct the first governmental interagency hospital managers' training institute October 3-21. Trainees will be assigned by the Army, Navy, Air Force, Public Health Service and Bureau of Indian Affairs, as well as the Veterans Administration. Lecturers and speakers will include Dr. Walter A. Bloedorn, dean of George Washington University School of Medicine; Dr. Warren Brown, associate dean of medicine at Baylor University; Dr. Paul R. Hawley, executive officer of Blue Cross and Blue Shield, and Dr. Perrin Long, Johns Hopkins University. The institute, which is to be held semiannually, is under the supervision of the Research and Education Service, headed by Dr. E. H. Cushing. Its primary aim is "to improve experienced administrators' knowledge of up-to-date personnel management practices and executive leadership."

Nine Institutions Receive New Cancer Grants

Grants in aid totaling $3,250,000 for assistance in construction of cancer research facilities were announced September 19 by the Federal Security Agency. Recipients are: University of Minnesota, $200,000, for two floors of clinical research at Mayo Memorial Medical Center; University of Chicago, $240,000, toward construction of the $2,000,000 Goldblatt Memorial Hospital for Cancer Research; New England Deaconess Hospital, $85,000, for an experimental detection center; University of Kansas, $200,000, for one wing of a two story building for laboratory and clinical research; Johns Hopkins University, $750,000, toward construction of cancer research facilities; St. Louis University, $625,000, for a clinical research building at the medical school; New York Memorial Hospital, $250,000, for a one floor addition to the experimental surgery laboratory;

University of California at Los Angeles, $700,000, for a laboratory research wing of the medical school, and University of Pennsylvania, $200,000, for a laboratory in the diagnostic clinic, which is being erected.

Conference on Veterans Hospitals

Persevering in his efforts to have the Veterans Administration proceed with a full scale hospital construction program, Senator Claude Pepper (Dem., Florida) presided at a special conference September 19 on possible means of ending the Administration's present retrenchment policy. Attending the executive session were Carl R. Gray Jr., administrator of veterans affairs; Fred A. McNamara, hospital expert of the United States Budget Bureau, and Representative John Rankin (Dem., Mississippi). The latter is chairman of the House Veterans Committee and, like Senator Pepper, has been attempting to have President Truman rescind his executive order of last January that the hospital construction program be reduced by 16,000 beds. No decisions were reached at the conference, but Capitol observers have no doubt that pressure will continue to be exerted on the White House, by veterans organizations as well as by many members of Congress, to modify the cutback order.

Number of Births Stays at 1948 Level

Public Health Service tabulations indicate that the number of live births in this country during the first six months of 1949 was approximately the same as for the corresponding period in 1948, but well below the 1947 figure. For 1949, it was 1,706,000; for 1948, the figure was 1,694,000, and for 1947, 1,865,881. Excluding armed forces overseas, the January-June rate this year is 23.1 per 1,000 population. For the comparable period last year the rate was 23.3. Surgeon General Leonard A. Scheele explained that, if unregistered births are included, the January-June figure for 1949 is estimated at 1,777,700, compared with 1,768,000 for the same period in 1948.

Dr. Wright Joins Schistosomiasis Group

Appointment of Dr. Willard H. Wright, of the National Institutes of Health, to membership on the Expert Committee on Schistosomiasis of the World Health Organization has been announced by the U. S. Public Health Service. The committee's first meeting is scheduled for October 24-29 in Cairo. Dr. Wright received the Legion of Merit for his work in World War II, while he was detailed to the Army, as an investigator of schistosomiasis problems in the Far East.

Emergency Care Unaffected by "Stop" Order

Suspension of payments from the United Mine Workers Welfare and Retirement Fund, which became effective September 17 as a result of diminishing revenues, does not apply to emergency hospital and medical services. The fund's trustees adopted a resolution which provides that payments for such services will continue to be made, "as determined by medical administrative officers of the Fund."

Report on Foreign Use of Radioisotopes

Since radioactive isotopes from the Oak Ridge "pile" became available in September 1947 for foreign distribution, 616 shipments have been made to 22 countries, according to the Atomic Energy Commission. All have been used in medical research and therapy and scientific investigations. Ninety per cent have been used in therapy or physiologic research.

Lynn Adams to Represent Mental Group in Washington

Lynn Adams has resigned as executive secretary of the Mental Hygiene Society of Maryland to become Washington representative of the National Committee for Mental Hygiene. His office is at the headquarters of the American Psychiatric Association.

Coming Medical Meetings

Annual Conference of State Secretaries and Editors, Chicago, A. M. A. Building, Nov. 3-4. Dr. George F. Lull, 535 N. Dearborn St., Chicago 10, Secretary.

Ambulatory Fracture Association, Toronto, Canada, Royal York Hotel, Oct. 24-27. Dr. H. W. Wellmerling, 120 S. LaSalle St., Chicago 3, Secretary.

American Academy of Ophthalmology and Otolaryngology, Chicago, Oct. 9-14. Dr. W. L. Benedict, 100 First Avenue Bldg., Rochester, Minn., Secretary.

American Academy of Pediatrics, San Francisco, Nov. 14-17. Dr. Clifford G. Grulee, 636 Church St., Evanston, Ill., Secretary.

American Clinical and Climatological Association, White Sulphur Springs, W. Va., The Greenbrier, Oct. 27-29. Dr. James Bordley III, Bassett Hospital, Cooperstown, N. Y., Secretary.

American College of Surgeons, Chicago, Stevens Hotel, Oct. 17-21. Dr. Paul B. Magnuson, 40 E. Erie St., Chicago 11, Secretary.

American Otorhinologic Society for the Advancement of Plastic and Reconstructive Surgery, Chicago, Palmer House, Oct. 13. Dr. Norman N. Smith, 291 Whitney Ave., New Haven 11, Conn., Secretary.

American Public Health Association, New York, Oct. 24-28. Dr. Reginald M. Atwater, 1790 Broadway, New York 19, Executive Secretary.

American Roentgen Ray Society, Cincinnati, Oct. 4-7. Dr. H. Dabney Kerr, University Hospitals, Iowa City, Iowa, Secretary.

American Society for the Study of Arteriosclerosis, Chicago, Hotel Knickerbocker, Nov. 5-7. Dr. O. J. Pollak, Quincy City Hospital, Quincy 69, Mass., Secretary.

American Society of Clinical Pathologists, Chicago, Drake Hotel, Oct. 11-15. Dr. C. G. Culbertson, 740 S. Alabama St., Indianapolis, Secretary.

American Society of Tropical Medicine, Memphis, Tenn., Nov. 6-9. Dr. Frederick J. Brady, National Institute of Health, Bethesda 14, Md., Secretary.

Association of Life Insurance Medical Directors of America, New York, Hotel Statler, Oct. 13-14. Dr. Henry B. Kirkland, P. O. Box 594, Newark 1, N. J., Secretary.

Association of Military Surgeons of the United States, Washington, D. C., Nov. 10-12. Col. James M. Phalen, Army Institute of Pathology, Washington 25, D. C., Secretary.

Central Society for Clinical Research, Chicago, Drake Hotel, Nov. 4-5. Dr. Kenneth G. Kohlstaedt, 960 Locke St., Indianapolis 7, Secretary.

Conference of State and Provincial Health Authorities of North America, New York, Oct. 28. Dr. Russell O. Saxvik, State Health Officer, Bismarck, N. D., Secretary.

Delaware, Medical Society of, Wilmington, Oct. 10-12. Dr. W. Edwin Bird, 822 North American Bldg., Wilmington, Executive Secretary.

District of Columbia, Medical Society of the, Washington, Hotel Statler, Oct. 17-19. Mr. Theodore Wiprud, 1718 M St. N.W., Washington 6, Secretary.

Gulf Coast Clinical Society, Pensacola, Fla., Oct. 6-7. Dr. Arthur J. Butt Jr., 1101 N. Palafox St., Pensacola, Fla., Secretary.

Inter-American Congress of Surgery, Chicago, John B. Murphy Memorial Auditorium, Oct. 21-23. Dr. Alton Ochsner, 1430 Tulane Ave., New Orleans, Chairman Program Committee.

International College of Surgeons, United States Chapter, Atlantic City, Haddon Hall, Nov. 7-12. Dr. Arnold S. Jackson, 1516 Lake Shore Drive, Chicago 10, Secretary.

Inter-State Post Graduate Medical Association of North America (International Medical Assembly), Philadelphia, Oct. 31-Nov. 3. Dr. Tom B. Throckmorton, Equitable Bldg., Des Moines, Iowa, Secretary.

Kansas City Southwest Clinical Society, Kansas City, Mo., Municipal Auditorium, Oct. 3-6. Dr. W. Merritt Ketchum, 630 Shukert Bldg., Kansas City, Mo., Secretary.

Kentucky State Medical Association, Owensboro, Oct. 6-9. Dr. Bruce Underwood, 620 S. Third St., Louisville 2, Secretary.

National Gastroenterological Association, Boston, Hotel Somerset, Oct. 24-26. Dr. Sigurd W. Johnsen, 1818 Broadway, New York 23, Secretary.

Neurosurgical Society of America, Quebec, Canada, Chateau Frontenac, Oct. 30-Nov. 1. Dr. Edward Schlesinger, 710 W. 168th St., New York, Secretary.

Oklahoma City Clinical Society, Oklahoma City, Biltmore Hotel, Oct. 24-27. Dr. F. Maxey Cooper, 512 Medical Arts Bldg., Oklahoma City, Director of Clinics.

Oregon State Medical Society, Eugene, Oct. 12-15. Dr. Werner E. Zeller, Medical-Dental Bldg., Portland 5, Secretary.

Southern Medical Association, Cincinnati, Nov. 14-17. Mr. C. P. Loranz, Empire Building, Birmingham, Ala., Secretary.

Southwestern Medical Association, Albuquerque, New Mexico, Nov. 9-12. Dr. Wickliffe R. Curtis, First National Bank Bldg., El Paso, Texas, Secretary.

Virginia, Medical Society of, Fort Monroe, Old Point Comfort, Oct. 9-12. Miss Agnes V. Edwards, 1200 E. Clay St., Richmond, Secretary.

Western Orthopedic Association, Santa Barbara, Calif., Biltmore Hotel, Oct. 19-21. Dr. Charles W. Gilfillan, 1680 N. Vine St., Hollywood, Calif., Secretary.

Wisconsin, State Medical Society of, Milwaukee, Hotel Schroeder and Milwaukee Auditorium, Oct. 3-5. Mr. Charles H. Crownhart, 704 E. Gorham St., Madison, Secretary.

World Medical Association, General Assembly, London, Eng., Oct. 10-15. Dr. Louis H. Bauer, 2 E. 103d St., New York City, Secretary General.

GOVERNMENT SERVICES

NAVY

ACTIVE DUTY WITH THE NAVAL AIR RESERVE TRAINING COMMAND

The Naval Air Reserve Training Command, with headquarters at Glenview, Ill., offers opportunities for active duty to inactive reserve medical officers and interested private physicians. Duty assignments are available at the following Naval Air Stations: Akron, Ohio; Atlanta, Ga.; Columbus, Ohio; Denver; Grosse Ile, Mich.; Lincoln, Neb.; Los Alamitos, Calif.; Niagara Falls, N. Y.; St. Louis; Spokane, Wash.; Willow Grove, Pa.; Jacksonville, Fla.; Minneapolis, and New Orleans. Those accepted for this duty will receive full base pay and allowances for subsistence and quarters commensurate with their rank; in addition, $100 per month will be paid to those who volunteer and agree to remain on active duty for a minimum of one year, as provided for by law. Moreover, qualified flight surgeons and aviation medical examiners will be issued orders to duty involving flying. Medical officers holding commissions in the Naval Reserve now on active duty may designate three stations in order of preference. Physicians who are not in the Naval Reserve may apply to their nearest Office of Naval Officer Procurement for information pertaining to securing a commission. Naval Reserve Medical Officers with the rank of lieutenant commander or below who wish to further their interest in aviation medicine may submit their request for the course given at the School of Aviation Medicine and Research, Naval Air Station, Pensacola, Fla. The request should include an agreement to remain on active duty for one year after completion of the course.

Inquiries should be directed to the Naval Air Reserve Training Command (Staff Medical Officer), Naval Air Station, Glenview, Ill., or to the Bureau of Medicine and Surgery (Division of Aviation Medicine), Navy Department, Washington 25, D. C.

SECOND ANNUAL SEMINAR

The second annual seminar in Military Medicine will be offered at the U. S. Naval Hospital, St. Albans, L. I., N. Y., Oct. 16-29, 1949. This course is intended to prepare students for duty in the event of a national emergency and to stimulate interest in the Naval Reserve. Lecturers will be chosen from the hospital staff and consultant physicians, Army and Navy medical departments. Medical officers of the Organized or Volunteer Reserve Corps may request two weeks' training duty with pay and allowances, including travel. Personnel having a claim pending for, or receiving, disability allowance, disability compensation or retired pay from the U. S. Government are not eligible for training duty with pay. Fourteen points toward the nondisability retirement plan will be credited each student.

COMMISSIONS IN THE NAVAL RESERVE

Because of the misinterpretation by some medical students concerning application for commissions in the Naval Medical Corps Reserve on graduation, as distinct and separate from the application for internship within Naval hospitals, the Surgeon General has forwarded the following statement:

Any student in a medical school approved by the Council on Medical Education and Hospitals of the American Medical Association, who meets the physical, citizenship and other requirements, may apply for a commission as Ensign, HP, U. S. Naval Reserve, at any time after his acceptance by such school. Those so appointed will be offered a subsequent appointment as Lieutenant, junior grade, Medical Corps Reserve, U. S. Naval Reserve, on graduation from an approved medical school. While it is not mandatory, it is desirable that those senior students who desire to apply for an internship in a Naval hospital, apply for a Reserve commission prior to the date of application for the internship in accord with the Cooperative Intern Placement Plan. This procedure will expedite the processing of applications for Naval internships in the one month period allowed under the Cooperative Intern Placement Plan. Selections for Naval internships will be made in accord with all provisions of the Cooperative Intern Placement Plan of the Association of American Medical Colleges, the details of which are available to the students through the dean of their medical school.

CAPT. JOEL J. WHITE RETIRES

Capt. Joel J. White, commanding officer, Naval Hospital of Chelsea, Mass., recently retired from active service in order to accept the medical directorship of the University of New Hampshire. As chief flight surgeon in the Surgeon General's Office he developed a carbon monoxide indicator which was considered the outstanding development in aviation in 1931. He performed outstanding services in World War I and World War II, and in the recent war he received the Navy Legion of Merit for actual combat in Guadalcanal. This citation entitled him to retire as rear admiral.

ADMIRAL BROWN APPOINTED INSPECTOR

Rear Admiral Clarence J. Brown (MC) has been appointed General Inspector of Medical Department Activities. He will also continue in his previous position of assistant chief of the Bureau of Medicine and Surgery for Research and Medical Military Specialties. Admiral Brown is a specialist certified by the American Board of Otolaryngology.

PERSONAL

Capt. James J. Sapero assumed his new duties as commanding officer, U. S. Naval Medical Research Unit 3, at Cairo, Egypt, succeeding Comdr. Robert A. Phillips, who became scientific director of the Research Unit.

Lieut. Comdr. Arthur V. Miller Jr., of Monroe, La., has been voluntarily recalled to active duty in the Medical Corps Reserve.

VETERANS ADMINISTRATION

INTER-AGENCY HOSPITAL MANAGERS INSTITUTE

The first governmental inter-agency hospital managers training institute will be conducted by the Veterans Administration October 3-21. Other participating agencies are the Department of the Army, Navy, Air Force, Public Health Service and the Indian Service. The institute will be held twice yearly, in February and October, and the program will be patterned after that which was conducted by the VA Department of Medicine and Surgery last February.

The training program is designed primarily to improve experienced administrators' knowledge of personnel management practices and executive leadership. The Training Division of the Personnel Relations and Training Service will lend technical assistance. The first phase of the program is the institute, which consists of lectures and study for three weeks. Immediately after the institute, the trainees are given two two-week assignments in hospitals managed by doctors with outstanding administrative ability. Finally, the trainees will be required, within six months after completion of the institute, to make trips to one or more hospitals in the vicinity of their own hospitals to keep abreast of good administrative technics. Each agency will select its participants in the program.

PERSONAL

Dr. Linus A. Zink has been appointed manager of the new Veterans Hospital in Brooklyn and Dr. Carleton Bates of the new hospital in Iron Mountain, Mich. Both are veterans of World War II.

PHYSICIANS SEPARATED FROM SERVICE

ARMY MEDICAL CORPS OFFICERS RECOMMENDED FOR/OR RELIEVED FROM ACTIVE DUTY

Montana

Lemire, Rosaire E. Jr.....Missoula
Stainsby, Donald L.....Great Falls

Nevada

Hawley, Robert L.....Reno
Moore, George Leland.....Elko

New Jersey

Alexander, James K.....Englewood
Allen, John Lewis.....Ocean City
Beshlin, William V.....Paterson
Boone, Alexander W. Jr.....Pennsgrove
Browdy, Sol.....Trenton
Cortelyou, Thomas P.....Princeton
Cozzarelli, James J.....Belleville
D'Alessandro, Genesio L.....Newark
Diorio, Carmine D.....Paterson
Fares, Louis G.....Trenton
Lyons, David R.....Newark
Mancusi-Ungaro, Alvin P.....Newark
Manowitz, Nelson.....Jersey City
Miller, Thomas E.....Nutley
Sakson, John A.....Trenton
Sarno, John A.....Newark
Shapiro, Henry D.....Paterson
Specht, Robert C.....East Orange

New Mexico

Stevens, D. D.....Roswell

New York

Auringer, E. M.....Addison
Avery, R. F.....Brooklyn
Bader, Mortimer E.....New York
Bader, Richard A.....New York
Barker, Charles P.....New York
Bartholomew, L. G.....Whitehall
Bell, H. M. Jr.....Massena
Beller, Martin L.....New York
Bellwin, A.....New York
Blair, Edwin.....Brooklyn
Blodgett, R. N.....Albion
Bowe, John Joseph.....Bronx
Brodoff, Stanley.....Bronx
Callas, Xenophen C.....Brooklyn
Cameron, Joseph J. Jr.....Brooklyn
Charlap, Myron.....New York
Cheiker, A.....Brooklyn
Chiaramonte, Joseph T.....Brooklyn
Christenson, Paul J.....Troy
Clark, William J.....Scarsdale
Coddington, Arthur M. Jr..Johnson City
Cohen, Clifford.....Brooklyn
D'Angio, G. J.....New York
Dann, H. A.....New York
Dattoli, John A.....Poughkeepsie
Dawson, Walter L.....Bronxville
De Vito, Nicholas John.....Forest Hills
Deyo, William B.....New York
Drachman, Stanley R.....New York
Dudasik, John J.....Brooklyn
Eby, Charles E.....New Rochelle
Edmonds, F. C. Jr.....Sea Cliff
Eisenbud, M.....New York
Emmel, R. C.....Mt. Vernon
Farrell, W. J.....Bronx
Feinberg, A. W.....Brooklyn
Ferber, Carl J.....Troy
Fisichella, R. A.....Brooklyn
Fitz, R. H.....Brooklyn
Fox, John R. Jr.....Rochester
Frankel, Jack.....Jamaica
Freundlich, Martin.....New York
Fretz, Alfred F.....Flushing
Friedman, C. R.....Brooklyn
Gahagan, Robert B.....Jackson Heights
Gelbard, David.....New York
Gilbert, Seymour C.....New York
Graceffo, J. F.....Auburn
Greenwald, Joseph C.....New York
Griffiths, R. B.....Amsterdam
Haggerty, Thomas E.....Brooklyn
Haynes, Douglas M.....New York
Henneman, Philip H.....Pelham
Herfort, Alan.....New York
Hewitt, Gerald.....Brooklyn
Hicks, Robert G.....New York
Holder, R.....New York
Hyams, George.....Brooklyn
Jacobius, Henry F.....New York
Joy, Charles A.....Fredonia
Keil, Frank C.....New York
Kelley, Gurney E.....Syracuse
Kerwin, Kenneth J.....Staten Island
Kesseler, Howard J.....New York
Kohn, M. Jr.....Schenectady
Kohn, Robert M.....Buffalo
Komora, Edward J., Jackson Heights, L. I.
Lampert, H.....Brooklyn
Landman, M. E.....Forest Hills
Norton, James J.....Utica
O'Keeffe, D. F.....North Creek
Olsen, Robert Clarence.....Brooklyn
Owre, E. S.....Staten Island
Palitz, S. F.....New York
Palumbo, V. A.....Brooklyn
Pannill, F. C. Jr.....New York
Pascale, Vincent H.....Bronxville
Siegman, Alfred J.....Brooklyn
Simson, J.....New York
Slowik, Rudolph F.....Utica
Wiggans, Roy G. Jr.....Ithaca
Wisoff, Carl P.....Neponsit
Wolkwitz, Robert E.....Brooklyn

North Carolina

Anderson, Robert H.....Wilson
Biles, Ervin W.....Charlotte
Bridger, Clarence E.....Winston-Salem
Clarke, James S.....Asheville
Dillard, Sam B.....Draper
Hallman, Bernard L.....Sanford
Highsmith, George P.....Dunn
Hubbell, David S.....Durham
Johnston, James W.....Elon College
Lee, Allen H.....Dunn
McIntosh, Archibald N.....Durham
Marks, Edgar S.....Greensboro
Nicholson, Neil G. Jr.....Rockingham
Phifer, William H.....Monroe
Shugart, Richard T.....Elkin
Suiter, Thomas B. Jr...Rocky Mountain

North Dakota

McDonald, William J.....Bismarck
Nordquist, Paul W.....Fargo
O'Brien, J. C.....Dickinson
Pile, D. F.....Mandan
Sommerness, M. D.....Columbus
Sterns, Donald.....Grand Forks

Ohio

Anderson, Rupert F. Jr.....Gambier
Apel, Otto F.....Portsmouth
Bennett, Albert R.....Columbus
Bond, William H.....Columbus
Bradford, G. T.....Cleveland
Brant, C. H.....Lakewood
Clapper, Henry H.....Akron
Clark, S. G.....Columbus
Clemente, Bartholomew.....Columbus
Cope, Jerome A.....Ravenna
Davis, E. C. Jr.....Dover
Davis, William M.....Akron
Di Salvo, Remo J.....Cincinnati
Dzurik, Frank J.....Cleveland
Emslie, R. J.....Cleveland
Farrell, Robert X.....Springfield
Feigert, Marion W.....Van Wert
Finck, S.....Cleveland
Fishman, Stanley I.....Cincinnati
Fouke, A. E.....Fremont
Franklin, John W. Jr.....Chillicothe
Fry, G. D.....Youngstown
Fuhs, J. C.....Cincinnati
Gallagher, Robert T.....Akron
Geiger, Paul E.....Toledo
Gorbach, A. C. Jr.....Vermillion
Guyselman, H. L.....Urbana
Hagans, James A.....Cincinnati
Hans, C. L.....Cincinnati
Haynes, E. R.....Newark
Heppl, John A.....Cleveland
Herman, R. J.....Toledo
Hodges, W. H. Jr.....Columbus
Hudec, John A.....Cleveland
Huston, Talmadge R.....Carey
Jackson, Charles E.....Dayton
Kilduff, James F. Jr.....Cleveland
Kosar, Joseph.....Medina
Lammers, G. P.....Leipsic
Lefevre, J. D.....Springfield
Lilly, John S.....London
McGarry, John F.....Wickliffe
Manthey, C. E.....Cleveland Heights
McGrew, C. A.....Canal Fulton
McKitrick, Charles J.....Cambridge
Masters, Francis Wynne.....Cleveland
Maurer, Frederic G. Jr.....Lima
Minnig, Donald I.....Akron
Mockbee, Charles W.....Cincinnati
Morey, Gordon R.....Cincinnati
Mulvaney, William P. Jr.....Cincinnati
Murphy, W. W.....Kent
Palay, S. L.....Cleveland
Pampush, James J.....Lakewood
Rauch, Robert F.....Lancaster
Reagan, Edgar Joseph.....Dayton
Roberts, D. A.....Dayton
Rogers, S. I.....Youngstown
Rosenblum, A. M. Jr.....Youngstown
Rubenstein, Eli.....Cincinnati
Sampsel, James W.....Cleveland
Shaw, William E.....Cincinnati
Spyker, Thomas Hugh.....Columbus
Swanson, Gerald W.....Columbus
Swartz, William T.....Cincinnati
Taylor, James A.....Bellefontaine
Van Noate, H. F.....Doylestown
Walkowiak, John E.....Cleveland
Wemmer, Keith S.....Toledo

Washington

Cox, Russell L.....Seattle
Decker, John P.....Spokane
Hemmen, John E.....Seattle
Keizur, Lowell W.....Longview
Krippaehne, William W.....Puyallup
LaJoie, William J.....Spokane
Levin, Floyd D.....Walla Walla
Mills, Albert V.....Bremerton

West Virginia

Berman, Ralph E.....Beckley
Mathias, James D.....Mathias
Potterfield, Thomas G.....Charleston
Stansbury, Fred Jr.....Beckley

Wyoming

Tebbet, R. D.....Torrington

Canal Zone

Shrapnel, B. C.....Armuella
Stevenson, G. M.....Ancon

Hawaii

Craig, R. L.....Honolulu
Thorup, Oscar A. Jr.....Honolulu

Puerto Rico

Hoyos-Napoleoni, Hector A.....Ponce
Yordan, E.....Ponce

Canada

Sacharoff, M.....Windsor

Wales

Fredman, R.....Cardiff

Medical News

(Physicians will confer a favor by sending for this department items of news of general interest: such as relate to society activities, new hospitals, education and public health. Programs should be received at least two weeks before the date of meeting.)

ARKANSAS

Postgraduate Course in Pediatrics.—The University of Arkansas School of Medicine, Little Rock, will present a postgraduate pediatric course on October 31 and November 1. Physicians, public health nurses and workers are invited to attend. Guest speakers will be Dr. Herbert C. Miller Jr., University of Kansas School of Medicine, Lawrence-Kansas City, and Dr. Harry Bakwin, New York University School of Medicine, New York. No fees will be charged.

CALIFORNIA

Symposium on Heart Disease.—The annual postgraduate symposium on heart disease presented by the Heart Division of the San Francisco Tuberculosis Association will be held at the St. Francis Hotel in San Francisco October 12-15. Dr. William Dock, Brooklyn, and Dr. Arnold R. Rich, Baltimore, will be the guest speakers. Two concurrent courses in electrocardiography, to be given the morning of October 12, have been added to the program this year; one is an elementary course and the other an advanced course. The Wednesday afternoon session is planned for pediatricians and will be sponsored by the American Academy of Pediatrics.

Consultative Tumor Clinic.—The University of Southern California School of Dentistry, Los Angeles, has opened its first Tumor Consultative Board and Clinic to provide a consultative service which any member of the dental or medical profession may attend with or without a patient for oral tumor diagnosis. Meetings will be held on Fridays from 9 to 11 a. m. at the Clinic Building, Sixteenth and Los Angeles Streets. The professional service is made available by the school of dentistry faculty with the cooperation of the U. S. Public Health Service and the American Cancer Society. Inquiries or appointments for patients should be directed to Miss Shirley J. Carson, Secretary, 122 East Sixteenth Street, Los Angeles.

COLORADO

Courses in Poliomyelitis.—Aided by a grant from the National Foundation for Infantile Paralysis, the University of Colorado Medical Center is continuing to offer to physicians a series of postgraduate courses on poliomyelitis. Emphasis will be placed on the comprehensive care of patients in an epidemic. The courses are open to physicians who are graduates of medical schools approved by the American Medical Association and who reside in states west of the Mississippi. Three one-week courses are scheduled: November 7-11, 1949; March 13-18, 1950, and May 22-27, 1950. For information, address the Director of Poliomyelitis Teaching Program, University of Colorado Medical Center, Denver.

DISTRICT OF COLUMBIA

Annual Scientific Meeting.—The annual scientific assembly of the Medical Society of the District of Columbia will hold its annual meeting at the Hotel Statler October 17-19. The program includes the following speakers:

Paul D. White, Boston, Etiology of Coronary Heart Disease.
George E. Burch, New Orleans, Management of Congestive Heart Failure.
Samuel Bellet, Philadelphia, Treatment of Cardiac Arrhythmias.
Robert R. Linton, Boston, Diseases of the Veins of the Lower Extremities and Their Treatment.
Edward A. Gall, Cincinnati, What Is Early Cancer?
Freddy Homburger, Boston, Modern Aspects of the Physiopathology of Cancer.
Elise Strang L'Espérance, New York, Detection and Prevention of Early Cancer.
Richard H. Chamberlain, Philadelphia, Radiotherapy in Treatment of Cancer.
Lawson Wilkins, Baltimore, Diagnosis and Management of Hypothyroidism in Childhood.
Jean Paul Pratt, Detroit, Use and Abuse of Estrogens.
John E. Howard, Baltimore, Male Hormone Deficiencies and Treatment.
Arthur J. Patek Jr., New York, Present Day Trends in the Treatment of Laennec's Cirrhosis.
Bruce K. Wiseman, Columbus, Ohio, Hypersplenism.
Charles G. Child III, New York, New Concepts in Surgery of the Pancreas.

FLORIDA

District Meetings.—The annual meetings of the Florida medical districts will be held October 24-28 in a city of each of the four districts. The Northwest Medical District meeting will be held in Quincy at the Swano Country Club. Dr. Edwin H. Andrews, Gainesville, has been invited to speak on "Consideration of the Pancreas in the Diagnosis of Upper Abdominal Diseases." The Northeast Medical District will meet October 26 at the Elks' Club in Palatka. The Southwest Medical District members, meeting October 27 at the Sebring Hotel, Sebring, will hear, among others, Dr. Garland M. Johnson, Fort Lauderdale, speaking by invitation on "The Toxic Effect of Tetra-Ethyl Pyrophosphate." At the Southeast Medical District meeting in Fort Lauderdale October 28 at the Trade Winds Hotel, Dr. Henry Fuller, Lakeland, has been invited to speak on "Observations on Digitoxin." All programs begin at 2:30 p. m. and are to be concluded with a dinner meeting.

ILLINOIS

Lectures on Ophthalmology and Otolaryngology.—The next meeting of the Central Illinois Society of Ophthalmology and Otolaryngology will be held at the Abraham Lincoln Hotel in Springfield, November 18-20. Dr. William L. Benedict, Rochester, Minn., will give lectures on "General Diseases: Ocular Manifestations" and "Tumors of the Eye and Orbit." Dr. Howard P. House, Los Angeles, will speak on "Indications and End Results of Fenestration Surgery," "Management of Otitis Media" and "Management of the Continually Stuffy Nose." Dr. Walter E. Owen, Peoria, a member of the society, will speak on: "Drug Therapy in Respiratory Allergy." Dr. Herbert R. Kobes, Springfield, will speak on the "State of Illinois Cooperates with the Ophthalmologist and Otolaryngologist."

Chicago

Wilder Memorial Lecture.—The fourth William Hamlin Wilder Memorial Lecture of the Institute of Medicine of Chicago will be delivered by Dr. Arthur J. Bedell, professor emeritus of ophthalmology, Albany (N. Y.) Medical College, at a joint meeting with the Chicago Ophthalmological Society October 14 at 8 p. m. in the Crystal Room of the Palmer House. The subject will be "Medical Ophthalmology: A Kodachrome Demonstration of Photographs of the Fundus in Diabetes, Hypertension, Nephritis, Optic Neuritis, and Choked Disk."

Heart Association Meeting.—The Chicago Heart Association will hold a clinical session in the Abbott Memorial Amphitheatre at Evanston Hospital, Evanston, October 13 from 10 a. m. to 12 noon. Subjects under discussion include "Treatment of Uremia by Dialysis Across the Intestinal Mucosa," "Hypertension and Effort in Cardiac Rupture Following Acute Myocardial Infarction," "Angiocardiography in the Adult" and "The Flow Property of Blood." The meeting will close with a clinicopathologic conference. All physicians are invited to attend.

University Appointments.—Dr. Aldo A. Luisada, instructor of physiology and pharmacology and lecturer in medicine at Tufts College Medical School, Boston, has been appointed to the staff of the Chicago Medical School as assistant professor of medicine and program director of cardiology. Dr. Luisada is a graduate of the Royal University of Florence Medical School and has held a number of professional posts in Italian universities and in the United States.——Dr. Nicolas Stefan Halmi, refugee Hungarian scientist, has been appointed instructor in anatomy at the University of Chicago. Dr. Halmi was on the faculty of medicine of the University at Pecs, Hungary, September 1947 to January 1949. He received his M.D. degree from the Peter Pázmány University in Budapest, 1947.

Lectures on Community Health.—A series of lectures sponsored by the University of Chicago will be presented on Tuesdays at 7:30 p. m. at the Woodrow Wilson Room, 116 South Michigan Avenue, on "Current Problems in Community Health." The program is as follows:

October 4, Voluntary Health Insurance Plans, Mr. George Cooley, American Medical Association.
October 18, General Principles Underlying Welfare Effort, Ernest E. Irons, President, American Medical Association.
October 25, Compulsory Health Insurance Plans, Alton A. Linford, Ph.D., University of Chicago.
Nov. 1, The Chicago and Cook County Health Survey: What Chicago is Doing, Mr. Robert E. Merriam.
Nov. 15, Industrial Health Program in Illinois, Frederick W. Slobe, Chicago Medical Society.
Nov. 29, Mental Hygiene Program in Illinois, Mr. Fred H. Hoehler, Department of Public Welfare, State of Illinois.
Dec. 6, The World Health Organization, Mrs. Louise L. Wright, Chicago Council on Foreign Relations.

A ticket for the series may be obtained for $4, single admission, 75c.

KANSAS

City Park Named for Veteran Doctor.—Over 1,000 residents of Northwest Kansas, Eastern Colorado and Southwestern Nebraska attended ceremonies August 28 dedicating Gulick Park in Goodland in honor of Dr. Arthur C. Gulick, physician in that city for nearly half a century. A number of speakers expressed the high esteem in which the doctor is held by his neighbors and friends. A radio phonograph equipped for television was presented to the doctor and his wife.

LOUISIANA

Legal Medicine Program Established.—A law-science program has been established at Tulane University of Louisiana, New Orleans, to bring about an effective integration between the fields of law and medicine on the graduate and undergraduate levels. Dr. Hubert Winston Smith, former professor of legal medicine at the University of Illinois, Chicago, has been named research professor of law and medicine. He will serve also as professor of law and professor of legal medicine in the college of law and school of medicine, respectively. New courses and seminars will be devoted to more complete training of trial lawyers in the science of proof and of handling personal injury litigation and in legal psychiatry. Long range plans call for projected developments in clinical legal medicine, legal pathology and scientific crime prevention and detection. A course in legal medicine has been established. It is planned also to offer a course in medicolegal aspects of behavior problems.

During the past few years Dr. Smith has been doing research with other specialists in reformulating medical sciences in terms of their legal applications and utility. The result has been publication of more than one hundred and twenty-five studies, in both medical and legal journals. During World War II Dr. Smith served as officer in charge of the legal medicine branch, Bureau of Medicine and Surgery, U. S. Navy.

MICHIGAN

Kresge Research Fund.—Wayne University College of Medicine, Detroit, has been granted $113,850 by the Kresge Foundation which will be known as the Kresge Research Fund. The grant, which is payable in installments of $37,950 over a three year period, is to be used for the study of revascularizing ischemic limbs and the study of the physiologic, anatomic and surgical possibilities of this technic. Drs. Charles G. Johnston and Prescott Jordan Jr., of the college faculty, are reported to have recently performed successfully an operation in which arteries were sutured into veins. Drs. John E. Webster, Elisha S. Gurdjian and Gordan H. Scott, Ph.D., are working with Drs. Johnston and Jordan in the investigation. This research will be carried on at the Wayne University College of Medicine, the City of Detroit Receiving Hospital and Grace Hospital. The Board of Education accepted the grant on August 23 on behalf of the medical school.

MONTANA

State Medical Election.—The Montana State Medical Association in July chose Dr. Clyde H. Frederickson, Missoula, as president-elect and installed Dr. Thomas F. Walker, Great Falls, as president. Dr. Herbert T. Caraway, Billings, was reelected secretary-treasurer.

NEW YORK

Postgraduate Lectures.—The Schenectady County Medical Society at the Eastern New York Orthopedic Hospital, Schenectady, October 4 at 8:30 p. m., will be addressed by Dr. Paul Reznikoff of New York on "Blood Dyscrasia Produced by Industrial Exposures." The Geneva Academy of Medicine will hear Dr. Arthur M. Reich, Scarsdale, speak on "The Treatment of Obstetrical Bleeding" at a meeting October 17 at 8:30 p. m. at the Bellhurst, Geneva. These lectures have been arranged by the Medical Society of the State of New York in cooperation with the New York State Department of Health.

New York City

Graduate Fortnight.—The New York Academy of Medicine will hold its twenty-second Graduate Fortnight October 10-21. These evening lectures at the Academy of Medicine Building begin at 8:30 p. m. Among the subjects to be discussed are present and prospective diagnostic uses of radioactive isotopes, electrolytes and electrocardiography, cardiac and renal disorders, liver disease, hematologic disorders, diagnostic cell-staining reactions, gastroenterologic disorders, neuropsychiatric disorders and bacterial and virus infections.

Appoint Executive Secretary of County Society.—Mr. Robert D. Potter of Scarborough-on-Hudson has been appointed as the new executive secretary of the Medical Society of the County of New York and editor of its journal, *New York Medicine*. Mr. Potter was executive director of the recent International Congress on Rheumatic Diseases. He has also been science editor of the *N. Y. Herald Tribune* and news editor of Science Service syndicate. He was a founder member of the National Association of Science Writers and has twice served as president of the organization.

Lectures for Laymen.—The New York Academy of Medicine Lectures to the Laity on "Frontiers in Medicine" began September 28 and will extend through January 25. They are held at the Academy of Medicine Building, 2 East 103 Street at 8:30 p. m. and will be broadcast by radio. Admission is free. The program is as follows:

Oct. 26, David Seegal, New York, Methuselah—Myth or Promise.
Nov. 16, Laurence H. Snyder, Sc.D., Oklahoma City, Anniversary Discourse of the Academy, Frontiers in Genetics.
Dec. 7, John H. Gibbon Jr., Philadelphia, Machines That Work Like Men.
Jan. 11, Selman A. Waksman, Ph.D., New Brunswick, N. J., Biology of the Antibiotics.
Jan. 25, Thomas M. Rivers, New York, The George R. Seidenburg Memorial Lecture, Concepts and Methods of Medical Research.

The lectures will be published by and copies may be purchased from the Columbia University Press, Columbia University, New York 27.

Venereal Disease Seminars.—A series of twelve weekly lectures and demonstrations on the diagnosis, treatment and management of venereal diseases will start at the New York City Department of Health October 8 at 10:30 a. m. in the second floor auditorium of the Health Department, 125 Worth Street. The schedule of lectures includes:

Oct. 8, Dr. Walter P. Anderton, Columbia University College of Physicians and Surgeons, The Medical Practitioner and Venereal Disease.
Oct. 15, Richard C. Arnold, Venereal Disease Research Laboratory, U. S. Public Health Service, Current Developments in the Treatment of Syphilis.
Oct. 22, Aaron Prigot, Harlem Hospital, Aureomycin in Venereal Disease.
Oct. 29, Frank C. Combes, New York University-Bellevue Medical School, Primary Syphilis.
Nov. 5, Royal M. Montgomery, New York Polyclinic Medical School and Hospital, Skin Lesions of Syphilis and Their Differential Diagnosis.
Nov. 12, Borris A. Kornblith, Gouverneur Hospital, Chancroid, Lymphogranuloma Venereum and Granuloma Inguinale.
Nov. 19, Edwin P. Maynard Jr., Long Island College of Medicine, Heart Disease and Syphilis in the General Practitioner's Office.
Nov. 26, Bernhard Dattner, Bellevue Hospital, Syphilis of the Central Nervous System.
Dec. 3, Charles R. Rein, New York University Bellevue Medical Center, Serodiagnosis of Syphilis.
Dec. 10, Hortense Hilbert, R.N., The Public Health Nurses' Role in the General Practitioner's Approach to Venereal Disease.
Dec. 17, Mortimer D. Speiser, New York University Medical School, The Syphilitic Pregnant Woman and Her Expected Child.

At a special meeting December 2, J. W. Richter, D.D.S., will speak on "The Oral Manifestations of Syphilis and Their Differential Diagnosis, of Interest to Medical and Dental Practitioners."

OHIO

Hoyt Memorial Loan Fund.—A memorial loan fund for medical students of orthopedics is to be established in Akron in honor of the late Dr. Walter A. Hoyt, former orthopedic surgeon on the staffs of City and Children's hospitals in Akron. Resident doctors at the two hospitals may use the fund for further study at the University of Pennsylvania, Philadelphia.

Hospital Lecture.—Dr. Leo G. Rigler, professor of radiology at the University of Minnesota Medical School, Minneapolis, will deliver the Annual Lectureship of Mount Sinai Hospital, Cleveland, in the Auditorium of the Residence Hall of the hospital October 6 at 8:30 p. m. on "Early Diagnosis of Carcinoma of the Lung." Dr. Rigler will hold a clinic at 3:15 p. m. This meeting is open to the medical profession.

PENNSYLVANIA

Environmental Cancer Study.—The Pennsylvania Department of Health will conduct a study of environmental cancer in Pennsylvania industry. It will include a statistical study and an environmental evaluation of all male cancer deaths which occurred in the general population of Pennsylvania during 1948 and a determination of the relative incidence of cancer in the various industries in the state. Dr. James D. Purvis has been named chief of the environmental cancer section, which has been established in the Bureau of Industrial Hygiene.

GENERAL

Wins Midwest Chemistry Award.—Robert D. Coghill, Ph.D., director of research, Abbott Laboratories, North Chicago, is the recipient of the 1949 Midwest Award of the St. Louis Section of the American Chemical Society, which will be presented at a dinner meeting in St. Louis October 3. The award is in recognition of "meritorious contribution to the advancement of pure or applied chemistry or chemical education" in his work in the development of large scale penicillin production technics.

Communicable Disease Report.—The U. S. Public Health Service announced September 14 that North Dakota had reported 6 cases of infectious encephalitis for the week ended September 10 as compared with 16 the previous week, and South Dakota reported 5 cases as compared with 1 the previous week. One hundred and fourteen cases of typhoid and paratyphoid fever were reported. The total to date is 2,602, as compared with 2,460 for the same period in 1948, which was a record low for the period. One case of smallpox was reported during the week in Kentucky.

International Medical Assembly.—The Interstate Postgraduate Medical Association of North America will hold its International Medical Assembly in the Public Auditorium, Philadelphia, October 31-November 1 under the presidency of Dr. Evarts A. Graham, St. Louis. Scientific papers and diagnostic clinics will be presented, beginning at 8:30 a. m. and extending into the evening. The award of the association's Medallion of Honor to Dr. Chevalier Jackson, honorary professor of bronchoesophagology at Temple University School of Medicine, Philadelphia, will be made Thursday afternoon. Technical and commercial exhibits will be displayed.

Clinical Pathologists Meeting.—The American Society of Clinical Pathologists will hold its annual meeting and seminar at the Drake Hotel, Chicago, October 12-15, under the presidency of Dr. O. A. Brines, Detroit. Those delivering papers by invitation include:

George Y. Shinowara, Ph.D., Columbus, Ohio, Prothrombin Level of Human Plasma.
Lester D. Odell, Chicago, Factors Affecting the Activity of Beta Glucuronidase in Gynecologic Tissues and Fluids.
Harold L. Stewart, Bethesda, Md., Pathology of Chemical Carcinogenesis.
Ross L. Gauld, Washington, D. C., Diagnosis of Viral and Rickettsial Diseases by Hospital Laboratory.
Henry Pinkerton, St. Louis, Morphology of Viral Inclusion Bodies and Their Practical Value in the Diagnosis of Viral Diseases.
James H. Peers, Bethesda, Md., Isoallergic Encephalitis and Its Possible Relation to Human Disease.

The Ward Burdick Award contribution will be given by Dr. Shields Warren, Boston, on the "Clinical Pathologist in the Atomic Age." On Wednesday at 9 a. m. there will be a panel discussion on Training of Residents, under the chairmanship of Dr. Frank W. Hartman, Detroit, sponsored by the society, the American Board of Pathology and the College of American Pathologists. In the afternoon there will be a symposium on "Methods for the Determination of Blood Sugar."

Lloyd Miller to Head U. S. P. Revision.—The U. S. Pharmacopeial Board of Trustees on September 17 elected Lloyd C. Miller, Ph.D., Rensselaer, N. Y., as director of pharmacopeial revision for the new decade, which will follow the meeting of the U. S. Pharmacopeial Convention in Washington in May, 1950. He will succeed the retiring chairman Dr. E. Fullerton Cook, who has been associated with the U. S. P. since 1901 and has served as chairman since 1920. Dr. Miller has been a member of the U. S. P. Revision Committee since 1944 and became chairman of the Subcommittee on Biologic Assays in 1946. A native of Illinois, Dr. Miller received his Ph.D. from the University of Rochester (N. Y.) School of Medicine and Dentistry in 1933 with a major in biochemistry. He was a research fellow at the Upjohn Company, serving in biochemistry, from 1935 to 1943. He worked with the Division of Pharmacology, U. S. Food and Drug Administration. Since 1944, following one year with the Winthrop Chemical Company, he has been director, Biology Division, Sterling-Winthrop Research Institute, Rensselaer, N. Y. His contact with U. S. P. activities embraces the U. S. P. XI, XII, XIII and XIV. The Ebert Prize of the American Pharmaceutical Association was awarded him in 1940 for research on the assay of digitalis. He is the author or co-author of many scientific papers on pharmaceutic research and has recently been appointed associate editor of the *Journal of Pharmacology and Experimental Therapeutics*.

Prevalence of Poliomyelitis.—Reports of cases of poliomyelitis for the periods indicated have been received from the National Office of Vital Statistics, U. S. Public Health Service.

Division and State	Week Ended Sept. 17, 1949	Week Ended Sept. 18, 1948	Median Expec.	Jan. 1 to Sept. 17, 1949	Jan. 1 to Sept. 18, 1948	Total * March 19 to Sept. 17, 1949	Total * March 20 to Sept. 18, 1948
New England States:							
Maine	50	1	2	358	29	358	29
New Hampshire	16	1	3	147	14	147	14
Vermont	12	..	..	90	15	88	14
Massachusetts	165	16	33	1,241	127	1,241	124
Rhode Island	17	1	1	94	2	94	2
Connecticut	56	5	12	390	74	387	73
Middle Atlantic States:							
New York	354	115	129	3,803	811	3,783	775
New Jersey	127	71	54	935	442	800	435
Pennsylvania	64	74	74	488	436	478	425
East North Central States:							
Ohio	146	149	118	1,216	767	1,210	758
Indiana	68	42	29	821	271	811	261
Illinois	196	99	90	2,191	615	2,175	608
Michigan	308	71	71	1,987†	397	1,967†	391
Wisconsin	64	46	39	652	284	648	284
West North Central States:							
Minnesota	150	115	40	1,357	673	1,318	665
Iowa	52	90	42	820	552	807	539
Missouri	60	28	24	1,053	178	1,042	178
North Dakota	35	12	5	309	85	305	85
South Dakota	23	55	1	271	158	249	158
Nebraska	46	60	18	401	421	388	416
Kansas	51	32	9	545	201	519	198
South Atlantic States:							
Delaware	3	8	6	38	112	36	111
Maryland	3	11	8	123†	50	114†	49
District of Columbia	8	12	5	67	85	66	85
Virginia	26	41	19	237	376	227	374
West Virginia	18	10	10	272	116	265	111
North Carolina	10	75	15	173	2,082	146	2,058
South Carolina	9	17	2	81	295	68	287
Georgia	8	7	5	143†	170	135†	169
Florida	14	10	10	181	195	169	178
East South Central States:							
Kentucky	32	11	11	426	142	418	139
Tennessee	27	38	12	398	267	392	260
Alabama	17	13	5	188	154	175	142
Mississippi	11	15	3	259	114	248	112
West South Central States:							
Arkansas	25	12	5	819	114	808	112
Louisiana	22	7	6	180	100	168	94
Oklahoma	50	19	11	1,067	290	1,000	284
Texas	52	42	10	1,786	1,407	1,695	1,386
Mountain States:							
Montana	7	2	3	53	43	52	33
Idaho	21	4	3	345	90	332	63
Wyoming	7	4	1	83	65	83	65
Colorado	54	7	7	459	76	457	74
New Mexico	16	4	4	131	56	130	54
Arizona	1	11	2	113	92	102	91
Utah	18	11	7	140	50	124	47
Nevada	..	..	..	11	3	11	2
Pacific States:							
Washington	39	19	19	381	156	336	138
Oregon	27	20	12	150	98	134	82
California	127	326	46	1,566	2,672	1,277	2,640
Total	2,612	1,839	.....	29,079†	16,022	28,163†	15,672
Median, 1944-1948	.....	.....	1,440	12,412		12,149	

* Last two columns show reported incidence since approximate average seasonal low: 26 weeks.

† Corrections (made in cumulative totals): Deductions, week ended September 10: Michigan 1 case, Georgia 3 cases. Additions: Maryland—4 cases July onset, 6 cases August onset. Weeks not specified.

LATIN AMERICA

Congress on Hygiene and Social Medicine.—The First Inter-American Congress and Second National Congress of Hygiene and Social Medicine will be held October 21-25 at Santa Fe City, Argentina, under the auspices of the Ministery of Public Health of Argentina and the Oficina Sanataria Panamericana. The program includes: Hernan Romero and Lorenzo García, "Standards for Preparation of Hygienists and Assistants in Sanitation," Miguel E. Bustamante and Antonio Velasco, "Technical Fundamentals and Administration of Centers of Health"; Fred L. Soper and Carlos A. Alvarado, "Campaign Against Insects, Vectors of Diseases"; Mollie Ray Carroll and Germinal Rodríguez, "Medico-Social Aspects of Social Insurance"; Dr. Francisco Pataro, "Absentism, in Industrial Hygiene," and Ramon Carrillo and Teófilo De Almeida, "General Principles of Architecture of Hospitals." Further information can be obtained from Dr. Luis M. Barreiro, General Secretary, San Jeronimo 1976, Santa Fe, Argentina, S. A.

Deaths

Gustavus Maximillian Blech ✦ Chicago; born in Riga, Latvia, Nov. 28, 1870; Barnes Medical College, St. Louis, 1894; veteran of the Spanish-American War; joined the Illinois National Guard and in 1913 organized the first Illinois field hospital, with which he served on the Mexican border in 1916; in 1917 served overseas as assistant division surgeon of the thirty-third division; commanded a hospital at Autun, France, and later was in charge of base hospital 208 at Bordeaux; discharged with the rank of colonel in 1919; in 1922 commissioned as colonel, medical reserve corps; member of the Association of Military Surgeons of the United States; past president of the Association of Military Surgeons of Illinois; honorary member of the Mexican Association of Military Surgeons; among the military and professional honors he received were the Legion of Honor from the Republic of France, the Grand Cross and Star, Order of St. Stanislaus by Czar Nicholas II of Imperial Russia, in recognition of suggestions for improvement of the Russian medical service when a Red Cross observer in 1904, on the Russian Japanese front; Commander, Order of St. George by the Kingdom of Belgium and Grand Cross and Star, Order of St. George; formerly professor of clinical surgery at Loyola University School of Medicine; consulting surgeon at the Cook County and Wesley Memorial hospitals; attending surgeon at the Edgewater Hospital; co-author with Col. Cornell C. Lynch of a volume entitled "Medical Tactics and Logistics"; in 1940 received the military surgeon's medal from the Mexican Ministry of National Defense; died August 9, aged 78, of coronary thrombosis, arteriosclerosis and cholelithiasis.

Hillyer Rudisill Jr. ✦ Charleston, S. C.; born in Macon, Ga., Feb. 28, 1902; Jefferson Medical College of Philadelphia, 1924; at one time instructor in radiology at the University of Chicago; part time associate professor of radiology at the Medical College of the State of South Carolina, which he joined as professor of radiology and electrotherapy, resigning in 1939 to accept a position as radiologist to Piedmont Hospital in Atlanta; served on the faculty of the University of Tennessee College of Medicine in Memphis, where he was on the staff of John Gaston Hospital; specialist certified by the American Board of Radiology; fellow of the American College of Physicians; member of the American Roentgen Ray Society and the American College of Radiology; for many years affiliated with the Roper Hospital; died July 27, aged 47, of coronary thrombosis.

J. Clifford Wallace, Fort Wayne, Ind.; born in Fort Wayne, Oct. 21, 1875; Fort Wayne College of Medicine, 1898; Rush Medical College, Chicago, 1900; member of the American Medical Association; formerly on the faculty of Fort Wayne College of Medicine; served on the city board of health and as school physician; an examiner for the Marine Corps for many years; on the examining boards during World Wars I and II; on the staffs of Lutheran and Methodist hospitals; member of the executive board of the Fort Wayne Medical Laboratory; died in St. Joseph's Hospital July 13, aged 73, of cardiovascular renal disease with hypertension.

Justin Orphus York, Santa Ana, Calif.; born in Panhandle, Texas, July 28, 1911; Louisiana University School of Medicine, New Orleans, 1940; served an internship and residency at Charity Hospital in New Orleans; entered the medical corps of the U. S. Naval Reserve in 1942 and served in the Pacific theater of operations until 1946; in March 1948 began active duty as a lieutenant commander in the medical corps of the U. S. Naval Reserve, assigned to U. S. Naval Hospital, Long Beach; died July 4, aged 37, of injuries received in an automobile accident.

James Greenwood ✦ Houston, Texas; University of Texas School of Medicine, Galveston, 1901; emeritus professor of neuropsychiatry at the Baylor University College of Medicine, where he was professor and chairman of the department of neuropsychiatry; past president of the Texas Neurological Society; member of the American Psychiatric Association and the Southern Psychiatric Association; medical director of Dr. Greenwood's Sanitarium; died August 22, aged 71, of arteriosclerotic cardiovascular disease.

Virginia Margaret Alexander ✦ Philadelphia; Woman's Medical College of Pennsylvania, Philadelphia, 1925; formerly medical adviser to Howard University in Washington, D. C.; during World War II served as a representative of the U. S. Public Health Service with the bituminous coal miners in Alabama; died in the University of Pennsylvania Hospital July 24, aged 50, of lobar pneumonia.

George Arthur Alliband ✦ Atlantic, Iowa; University of Nebraska College of Medicine, 1904; formerly city health officer; affiliated with Atlantic Memorial Hospital, where he died July 18, aged 74, of heart disease.

Clement Harrisse Arnold, Palo Alto, Calif.; Johns Hopkins University School of Medicine, Baltimore, 1918; on the staff of Palo Alto Hospital; died July 9, aged 64, of heart disease.

Maurice Asher, Maplewood, N. J.; University of the City of New York Medical Department, New York, 1893; also a graduate in pharmacy; served during World War I; died July 9, aged 84.

Harry Abraham David Baer ✦ Allentown, Pa.; Jefferson Medical College of Philadelphia, 1917; served during World War I; formerly owner of a hospital bearing his name; died in Allentown Hospital July 15, aged 61, of cerebral hemorrhage.

LeRoy Harrison Bailey, Los Angeles; New York Homeopathic Medical College and Flower Hospital, New York, 1913; served during World War I; staff physician in the city schools; died in the Hospital of the Good Samaritan July 5, aged 59, of hypertension and dissecting aortic aneurysm.

Joseph John Bailo, Windsor Locks, Conn.; Marquette University School of Medicine, Milwaukee, 1946; served during World War II; interned at St. Francis Hospital in Hartford, where he died June 26, aged 27.

Campbell Atkinson Baird, Mount Airy, N. C.; North Carolina Medical College, Davidson, 1904; died in the Williamsport (Pa.) Hospital July 23, aged 78, of acute coronary thrombosis.

James Henry Morgan Barber, Washington, D. C.; Georgetown University School of Medicine, Washington, 1888; member of the American Medical Association; died July 11, aged 83.

George Harbert Bartholomew, Los Angeles (licensed in California in 1918); died in California Lutheran Hospital July 11, aged 57, of pulmonary embolus.

Joseph John Bateman ✦ Washington, D. C.; Loyola University School of Medicine, Chicago, 1919; died in the Georgetown University Hospital July 18, aged 64, of coronary thrombosis.

Marshall Rowles Beard, San Fernando, Calif.; McGill University Faculty of Medicine, Montreal, Que., Canada, 1938; member of the American Medical Association and of the American Trudeau Society; served a residency at the Olive View (Calif.) Sanatorium; died July 25, aged 37.

Joseph Fortunat Belanger, Providence, R. I.; Laval University Faculty of Medicine, Quebec, Canada, 1913; died July 12, aged 64.

William Alexander Bevard, Washington, D. C.; National University Medical Department, Washington, 1894; for many years assistant medical officer in the Labor Department; died July 14, aged 90, of cerebral hemorrhage.

Frederick Egbert Bigelow, Chicago; Rush Medical College, Chicago, 1897; died in the Illinois Central Hospital July 5, aged 79, of cerebral hemorrhage, pneumonia and hypertension.

Robert Knox Bingham, Boone, N. C.; University of Tennessee Medical Department, Nashville, 1905; attending physician, Watauga Hospital; died in Davis Hospital, Statesville, July 30, aged 71, of sarcoma of the head of the pancreas.

Charles Alva Blayney, Penfield, Pa.; Jefferson Medical College of Philadelphia, 1900; member of the American Medical Association; for many years store physician at Gimbel Brothers; received an honorary degree of doctor of science from Waynesburg (Pa.) College in 1943; died in the Philadelphia General Hospital July 11, aged 80, of carcinoma of the pancreas with metastases.

Winfred Reynolds Blume ✦ Sioux City, Iowa; University of Nebraska College of Medicine, Omaha, 1930; affiliated with Lutheran, St. Joseph, Mercy and St. Vincent's hospitals; died July 21, aged 47, of acute coronary occlusion.

Arthur Francis Boell, Detroit; University of Michigan Medical School, Ann Arbor, 1921; member of the American Medical Association; fellow of the American College of Surgeons; affiliated with Mount Carmel Mercy and St. Joseph's Mercy hospitals; died July 21, aged 53, of heart disease.

Siegfried Boxer, New York; Medizinische Fakultät der Universität, Wien, Austria, 1902; died in Mount Sinai Hospital July 7, aged 71, of myocardial infarction and anemia due to gastrointestinal hemorrhage.

William Frederick Bruns, Ceredo, W. Va.; Eclectic Medical Institute, Cincinnati, 1888; member of the American Medical Association; formerly a member of the board of education for the Ceredo-Kenova Independent School District, serving as its president; died July 6, aged 83, of myocarditis.

Thomas Ambrose Buchanan, Oklahoma City; College of Physicians and Surgeons of Chicago, School of Medicine of the University of Illinois, 1903; for many years surgeon for the Santa Fe Railroad; died in Manitou Springs, Colo., July 31, aged 72, of coronary thrombosis.

John William Buehler, Aromas, Calif.; Chicago Homeopathic Medical College, 1895; affiliated with the Watsonville (Calif.) Hospital, where he died July 3, aged 80, of cerebral thrombosis.

Edward Kimball Burbeck ✦ Marblehead, Mass.; Johns Hopkins University School of Medicine, Baltimore, 1907; affiliated with Mary Alley Emergency Hospital; died July 1, aged 69, of coronary thrombosis.

Thomas Aloysius Burke ✦ Cleveland; Western Reserve University Medical Department, Cleveland, 1888; member of the American Academy of Ophthalmology and Otolaryngology; died in St. Mary's Hospital, Duluth, Minn., July 18, aged 85, following an appendectomy.

Norman Leonard Burnham ✦ Buffalo; University of Buffalo School of Medicine, 1896; formerly assistant professor of medicine at his alma mater; served as examiner on draft boards during World Wars I and II, for which he was awarded the service citation; for many years associated with Buffalo General Hospital, where he died July 21, aged 81, of carcinoma of the bladder and adenoma of the prostate.

Herbert Arthur Burns ✦ Anoka, Minn.; University of Minnesota College of Medicine and Surgery, Minneapolis, 1908; member of the American College of Chest Physicians; served during World Wars I and II; formerly medical superintendent of the Minnesota State Sanatorium at Ah-gwah-ching; chief of tuberculosis control unit, division of institutions for the state of Minnesota; died in the Veterans Administration Hospital, Minneapolis, July 8, aged 66.

Edmund Bradford Burwell, Tacoma, Wash.; University of Virginia Department of Medicine, Charlottesville, 1900; died in St. Joseph's Hospital July 17, aged 72, of auricular fibrillation and arteriosclerosis.

Frederick Leonard Case, Columbus, Ohio; Ohio Medical University, Columbus, 1900; served on the staff of the Mount Carmel Hosital; died July 7, aged 87.

Samuel C. Cawthorn, West Ridge, Ark.; Vanderbilt University School of Medicine, Nashville, Tenn., 1891; died July 21, aged 90.

Walter B. Christophel, Mishawaka, Ind.; Northwestern University Medical School, Chicago, 1909; served as president of the Mishawaka Chamber of Commerce; died July 21, aged 69, of cerebral hemorrhage.

Reamer Lorenza Cockfield, Lake City, S. C.; University of the South Medical Department, Sewanee, Tenn., 1908; Medical College of the State of South Carolina, Charleston, 1909; member of the American Medical Association; formerly city councilman and chairman of the city board of health; died in McLeod Infirmary, Florence, July 7, aged 65, of coronary thrombosis.

Lazarus N. Cohler, Chicago; University of Illinois College of Medicine, Chicago, 1915; member of the American Medical Association; died in the American Hospital July 27, aged 56, of chronic cholecystitis and cholelithiasis.

Carroll Dunham Conard, Mount Vernon, Ohio; Cleveland-Pulte Medical College, 1914; member of the American Medical Association; served during World War I; died July 26, aged 57.

Ernest Cooper, Miami, Fla.; Medical College of Indiana, Indianapolis, 1898; at one time practiced at Plainfield, Ind., at which time he was president of the Hendricks County Medical Society; died July 23, aged 79, of coronary thrombosis.

Marion Franklin Cruze, Powell Station, Tenn.; Tennessee Medical College, Knoxville, 1909; for many years justice of the peace; died in St. Mary's Memorial Hospital, Knoxville, July 27, aged 65, of uremia.

Lloyd Glenn Dack, St. Paul; University of Minnesota Medical School, Minneapolis, 1916; member of the American Medical Association; specialist certified by the American Board of Ophthalmology; affiliated with the Children's Hospital, Gillette State Hospital for Crippled Children and Mounds Park Hospital; died July 9, aged 59, of coronary thrombosis.

Andrew V. Dahlberg ✦ Chicago; Bennett Medical College, Chicago, 1906; founder and chairman of the board of directors of the South Shore Hospital, where he died July 22, aged 74, of carcinoma of the pancreas.

Richard E. Davies ✦ Waukesha, Wis.; Rush Medical College, Chicago, 1896; an Associate Fellow of the American Medical Association; served overseas during World War I; affiliated with Waukesha Memorial Hospital, where he died July 26, aged 78, of cardiovascular renal disease.

George Carlon Davis, Gillett, Ark. (licensed in Arkansas in 1909); member of the American Medical Association; died July 1, aged 65.

Edward Owens Day, Little Rock, Ark.; University of Arkansas School of Medicine, Little Rock, 1912; member of the American Medical Association; served during World War I; affiliated with St. Vincent's, Baptist and University hospitals; died in the Army and Navy Hospital in Hot Springs July 18, aged 66, of congestive heart failure.

Albert D. De Haven, Xenia, Ohio; Bennett College of Eclectic Medicine and Surgery, Chicago, 1888; member of the American Medical Association; formerly city commissioner, city health commissioner; member of the city council and mayor; for many years examiner for the Metropolitan Life Insurance Company; died July 23, aged 83; of uremia and arteriosclerosis.

Arlendo Irvin Dennison, McKenzie, Tenn.; University of Tennessee Medical Department, Nashville, 1904; died July 20, aged 75, of cerebral hemorrhage.

Johnson Frank Ditto, Portland, Ore.; St. Louis College of Physicians and Surgeons, 1915; member of the American Medical Association; affiliated with Portland Sanitarium and Hospital; died July 12, aged 67, of coronary thrombosis.

Dan Caldwell Donald Jr., Philadelphia; Harvard Medical School, Boston, 1947; resident in neurology at Jefferson Medical College Hospital; killed near Whitehall, N. Y., July 25, aged 25, when an airplane crashed.

Rex Dowler Duncan ✦ Los Angeles; University of Southern California College of Medicine, Los Angeles, 1909; affiliated with the Los Angeles General Hospital; died in July, aged 63.

William Ambrose Dunn, Boston; University of the City of New York Medical Department, 1893; member of the American Medical Association; served as police surgeon and as physician to the city prison; died in City Hospital July 14, aged 90, of arteriosclerosis and a fractured femur received in a fall at home.

Elsworth De Marr Erskine, Steubenville, Ohio; Baltimore Medical College, 1893; served during World War I; died in the Veterans Administration Hospital, Aspinwall, Pa., July 8, aged 79, of an infected cyst of the lung.

Robert Howard Eveleth, Roseville, Calif.; Hahnemann Medical College of the Pacific, San Francisco, 1906; city health officer; on the senior staff of Sutter Hospital, Sacramento; died July 15, aged 69, of cardiac failure and nephrosis.

Abraham R. Fellman, Beverly Hills, Calif.; Detroit College of Medicine, 1913; at one time on the staff of Grace Hospital in Detroit; died July 21, aged 59, of heart disease.

Frederick Laurence Flynn, St. Petersburg, Fla.; Georgetown University School of Medicine, Washington, D. C., 1943; member of the American Medical Association; certified by the National Board of Medical Examiners; on the staffs of Mound Park Hospital and St. Anthony's Hospital, where he died July 12, aged 40, of coronary occlusion.

David Ingham Frey ✦ New York; Columbia University College of Physicians and Surgeons, New York, 1904; served during World War I; consultant in pediatrics at Bronx Hospital, where he died July 25, aged 67, of cerebral hemorrhage.

Fred Maxwell Galloway, Lynbrook, N. Y.; Long Island College Hospital, Brooklyn, 1906; served as police surgeon and health officer; formerly practiced in Brooklyn, where he was on the staffs of the Bushwick, Samaritan and Kings County hospitals; past president of the medical board of Mercy Hospital; on the staff of the South Nassau Communities Hospital in Rockville Centre; died July 19, aged 65, of coronary thrombosis.

Daniel J. Gilbert, Port Byron, N. Y.; University of the City of New York Medical Department, 1890; health officer of the towns of Montezuma, Throop and Conquest; died in the Auburn City (N. Y.) Hospital July 29, aged 83, of bronchopneumonitis and myocardial degeneration.

Edward John Godfrey ✦ Waterbury, Conn.; Georgetown University School of Medicine, Washington, D. C., 1915; member of the New England Dermatological Society and the Ameri-

can Public Health Association; health officer; affiliated with St. Mary's Hospital; died July 2, aged 62, of coronary occlusion.

John James Wilson Grimes, Chicago; Loyola University School of Medicine, Chicago, 1922; member of the American Medical Association; for many years affiliated with the Municipal Tuberculosis Sanitarium; died in Sacred Heart Sanitarium, Milwaukee, July 7, aged 67.

Govan B. Harley, Dorchester, S. C.; Chattanooga (Tenn.) Medical College, 1898; died July 28, aged, 86, of coronary thrombosis.

Eugene Hemmeger, Adelphi, Ohio; Starling Medical College, Columbus, 1895; member of the American Medical Association; president and director of the Adelphi Banking Company; died July 22, aged 75, of coronary thrombosis.

Rayburn Nelson Joyner, Marianna, Fla.; Duke University School of Medicine, Durham, N. C., 1933; member of the American Medical Association; served as director of the Jackson County health department; died July 9, aged 37, of heart disease.

Herman Roscoe Kauffman ✦ Toledo, Ore.; Ohio Medical University, Columbus, 1904; served during World War I; at various times state senator, mayor and health officer; affiliated with Lincoln Hospital; died July 7, aged 70, of coronary thrombosis.

Richard Kehrmann, Oteen, N. C.; Christian-Albrechts-Universität Medizinische Fakultät, Kiel, Prussia, Germany, 1914; affiliated with the Veterans Administration Hospital; died at Soco Gap, Waynesville, July 4, aged 61, in an automobile accident.

Rube Crow Kennerly, Camden, Ark.; College of Physicians and Surgeons, Little Rock, 1909; member of the American Medical Association; county health officer and director of district number 7; died in Camden Hospital July 28, aged 66, of heart disease and uremia.

David Terry Kimbrough, Nashville, Tenn.; University of Nashville Medical Department, 1897; for many years associated with Veterans Administration hospitals at various places; died July 29, aged 76, of carcinoma of a bronchus.

Ernest Thomas Kinsey, Madison, Fla.; Georgia College of Eclectic Medicine and Surgery, Atlanta, 1914; member of the American Medical Association; died in Miami July 25, aged 57, of cerebral hemorrhage.

Milton Klein ✦ Dover, N. J.; Creighton University School of Medicine, Omaha, 1934; died July 12, aged 37, following an operation for removal of a pituitary adenoma.

Howard Andrew Knox ✦ New Hampton, N. J.; Dartmouth Medical School, Hanover, N. H., 1908; former officer in the U. S. Army reserve; served in the Mexican campaign; at one time an assistant surgeon in the U. S. Public Health Service attached to the immigration service; died in the Jersey City Medical Center, Jersey City, July 27, aged 64, of arteriosclerosis.

Thaddeus Marion Koppa, Dallas, Texas; University of Illinois College of Medicine, Chicago, 1933; member of the American Trudeau Society; formerly director of the bureau of epidemiology and the tuberculosis division of the bureau, state department of public health of Michigan; at one time director of the bureau of communicable diseases of the Wyoming State Department of Health; affiliated with the Veterans Administration; died in Kerrville July 22, aged 40, of coronary thrombosis.

Frank John LaRue, Elberta, Mich.; Grand Rapids Medical College, 1906; died in the University Hospital, Ann Arbor, June 9, aged 77, of coronary occlusion and hepatocellular carcinoma with metastases to both lungs.

Joseph F. Lauvetz, Wahoo, Neb.; John A. Creighton Medical College, Omaha, 1905; member of the American Medical Association; served as county and city physician; a director of the Wahoo State Bank; affiliated with St. Catherine's Hospital and Creighton Memorial St. Joseph's Hospital in Omaha; died in Omaha July 27, aged 64, of coronary disease.

Harold Theron Lehmann, Socorro, N. Mex.; University of Oklahoma School of Medicine, Oklahoma City, 1940; died July 21, aged 45, of coronary thrombosis.

Joseph Leland, Birmingham, Ala.; Tulane University of Louisiana School of Medicine, New Orleans, 1904; member of the American Medical Association; on the staff of Jefferson-Hillman Hospital; died July 23, aged 67.

Harry Leshin ✦ Hightstown, N. J.; Long Island College Hospital, Brooklyn, 1920; on the staffs of the William McKinley Memorial and St. Francis hospitals and the Mercer Hospital in Trenton; died in the New York Post Graduate Medical School and Hospital, New York, July 26, aged 52.

John Sidney McCafferty ✦ Freeport, Pa.; University of Pittsburgh School of Medicine, 1933; served during World War II; affiliated with the Allegheny Valley Hospital in Tarentum; died in Montreal, Canada, July 3, aged 40, of heart disease.

Greene Day McCall, Fulton, Mo.; Barnes Medical College, St. Louis, 1895; member of the American Medical Association; fellow of the American College of Surgeons; served during the Spanish American War and World War I; for many years physician for the Missouri School for the Deaf and Dumb; died July 22, aged 75, of heart disease.

Samuel Lloyd McCarthy, Altoona, Pa.; Jefferson Medical College of Philadelphia, 1905; died in the Altoona Hospital July 19, aged 69, of cardiac decompensation.

Guy Leroy Millington, Girard, Kan.; Homeopathic Medical College of Missouri, St. Louis, 1900; member of the American Medical Association; served as health officer of Sumner and Crawford counties; at one time a member of the state board of medical registration and examination; died in Girard General Hospital, recently, aged 70.

Sidney Mitchell, Plattsburg, N. Y.; University of Vermont College of Medicine, Burlington, 1906; past president of the Clinton County Medical Society; member of the American Medical Association; served during World War I; affiliated with Champlain Valley Hospital and Physicians Hospital, where he died July 26, aged 68, of cerebral thrombosis.

Gregory Leo Robillard ✦ Brooklyn; Fordham University School of Medicine, New York, 1918; fellow of the American College of Surgeons; member of the American Association of Industrial Physicians and Surgeons; for many years assistant medical examiner of Richmond County; served during World War I; affiliated with Norwegian Lutheran Deaconesses' Home and Hospital, Victory Memorial Hospital and Brooklyn Cancer Institute; died July 2, aged 54, of coronary disease.

John C. Russell, Saranac Lake, N. Y.; University of the City of New York Medical Department, New York, 1886; served as president of the village; past president and for many years member of the school board; in January 1948 resigned as president of the Saranac Lake Federal Savings and Loan Association, which he continued to serve as director until the time of his death; affiliated with Saranac Lake General Hospital; died July 10, aged 87, of arteriosclerosis.

William Warren Spiro, Long Island City, N. Y.; University and Bellevue Hospital Medical College, New York, 1904; member of the American Medical Association; affiliated with the Doctors Hospital, where he died July 13, aged 67, of cerebral hemorrhage.

George Albert Spray ✦ Wichita, Kan.; University Medical College of Kansas City, Mo., 1911; affiliated with Wesley, St. Joseph and St. Francis hospitals; died July 21, aged 68, of coronary occlusion.

Charles W. Thierry, Jr., St. Louis; Washington University School of Medicine, St. Louis, 1898; member of the American Psychiatric Association; formerly affiliated with St. Vincent's Sanitarium and the City Sanitarium; died in the Malcolm A. Bliss Psychopathic Institute July 23, aged 74.

Charles R. Treat, Sharon, Wis.; Chicago Homeopathic Medical College, 1888; member of the American Medical Association; died July 4, aged 83, of heart disease.

Leonidas C. Walker, Jamestown, Ohio; the Hahnemann Medical College and Hospital, Chicago, 1882; served on the school board and city council; died in Xenia, July 1, aged 94, following fracture of his hip in a fall.

Harry Claud Warren ✦ San Francisco; University of California Medical School, San Francisco, 1904; first vice president of the American College of Chest Physicians; member of the American Trudeau Society; died in St. Luke's Hospital July 29, aged 67.

George Waters ✦ Port Huron, Mich.; Detroit College of Medicine, 1903; member of the American Trudeau Society; served as acting assistant surgeon in the U. S. Public Health Service; affiliated with Port Huron Hospital, where he died July 4, aged 75, of myocarditis.

Emmett Burns Whigam, Akron, Ohio; Cleveland Medical College, 1895; police and fire physician for many years; died July 6, aged 76, of coronary sclerosis.

James P. Will, Jackson, Mich.; Michigan College of Medicine and Surgery, Detroit, 1897; died July 1, aged 83, of diabetes mellitus and arteriosclerosis.

Foreign Letters

ITALY

(From Our Regular Correspondent)

FLORENCE, Aug. 15, 1949.

Action of Anesthetics Augmented by Vitamin B_1

At the Medicosurgical Society of the Romagna, Dr. Neri and Dr. Bazzocchi discussed the augmented action of anesthetics by vitamin B_1. In his experimental and clinical research Dr. Neri used anesthetics either by local infiltration or by spinal anesthesia after an adequate amount of vitamin B_1 had been added to the anesthetic solution. He observed that the concentration of the anesthetic drug could be decreased to about one-third or one-half while the anesthetic effect remained the same.

Dr. Bazzocchi carried out experiments on the sciatic nerve of rabbits, based on the concept demonstrated experimentally by him and by Professor Donaggio that the anesthesia represents a reversible change; he observed that the vitamin B_1, which by itself does not exert any analgesic effect when brought in contact with the isolated sciatic nerve, speeds up and prolongs the action of an anesthetic. These experimental findings were confirmed by the clinical application of anesthetics by local infiltration or by spinal anesthesia. Vitamin B_1 alone, when used intravenously, does not exert any anesthetic effect but, according to the speaker, renders the subject more excitable.

The results of this research were published in Italian medical periodicals, and some hospitals have since employed this method, the results of which will be followed up by Professor Paolucci, director of the surgical clinic of the university in Rome.

In 1948 work was done at the University of Padua, by application of the solution to the cornea, but according to the speaker this was not done with the proper technic and the results did not accord with those previously reported. Further results obtained by the speaker were published in the *Journal of the International College of Surgeons*. There are also favorable French reports, and the results have received confirmation by Leger and Lange.

Under the supervision of Professor Paolucci, studies are now in progress on the employment of vitamin B_1 in peridural anesthesia, in which a reduction of the amount of the highly concentrated anesthetic solution which has been in use and accelerated action would be advantageous.

The mechanism through which vitamin B_1 exerts its action on the anesthetic still is not fully understood. Dr. Bazzocchi and Dr. Bocchetti believe that interference with tissue respiration is involved. One may, for instance, consider an action of the mordant type by which the vitamin B_1 may render the nerve more sensitive or by which the nerve bundles may make better use of the anesthetic substance.

Conference Held by Dr. Leonard A. Scheele

Dr. Leonard Scheele, Surgeon General, United States Public Health Service, and head of the United States delegation to the World Health Congress, held a conference in Rome, discussing the organization of the Public Health Service. He described the Public Health Service of the United States as the most important American state organization which is devoted to the health standards of the people. Its functions are similar to those exercised in Italy by the Office of the High Commissioner for Hygiene and Public Health, but, although it represents an autonomous entity, it forms a part of the Federal Security Agency, which is in charge of effectuating the programs of the government concerning social assistance, instructions, welfare and public health.

Deaths

The sudden death of Prof. Giulio Andrea Pari, director of the Institute of Medical Pathology of Padua University, has been announced. Professor Pari was born in Udine in 1880. As a student he became interested in the study of physiology, and, after receiving a doctor's degree, he continued to study at the physiologic institute of Padua under the directorship of Professor Stefani until he was given the right to hold university courses. He then became assistant and associate professor of pathology at the same university, having as his chief Prof. Luigi Lucatello.

He went to Vienna and became a pupil of Von Noorden, Falta and Siegmund, and in Bonn he studied with Ribbert and Flügge; returning to his homeland after this apprenticeship, he proved to be a brilliant investigator in both clinical and pathologic work. From 1925 until his death he had the chair of medical pathology in Padua. He published about one hundred and thirty scientific papers. Among his most important contributions are those concerning the physiology of the nerve centers; phenomena of excitability, of response to stimuli, of fatigue and of restoration of the centers of reflex, and the pathogenesis of Cheyne-Stokes phenomenon.

SWITZERLAND

(From a Special Correspondent)

July 19, 1949.

Medicine in War

The sessions at the Diplomatic Conference of Geneva are interesting to the medical profession because of the discussions on medical problems which arise especially during war. The majority of the points studied have been under consideration by the Medico-Juridical Commission, which met almost fifteen years ago in Monaco. Approved were proposals for improvement in the treatment of prisoners of war so that they will be assured care by physicians of their own nationality and effective protection of the civil population, women, old persons and children, from war operations and bombardments. Originality lies in the creation of "immune" medical localities for injured military personnel and of places and zones for the safety of civilians who do not participate in any way in the war effort of the belligerents.

Several interesting problems remain for solution. One is concerned with the freedom of medical personnel. To improve the treatment of injured military personnel, it will be necessary to provide immunity (neutrality) to nurses, to hospital personnel and particularly to physicians who take care of the wounded. Dunant, the Genevan founder of the Red Cross, spoke of "neutralization" to describe this immunity. He applied to human beings an expression which jurists of international law have reserved for territories.

In this manner the principle of noncaptivity of medical personnel was established. This idea has been followed as a sacred principle of the conferences of Geneva, during conventions held from 1864 to 1929, the date of the convention the principles of which are still in force.

In 1947, during a conference of government representatives who met in the offices of the International Committee of the Red Cross, this principle was contradicted for the first time. On the initiative of the delegates of the United Kingdom, Canada and the United States, who recalled the experience of the first world war and the inadequacy of the medical care in the prisoner of war camps, it was accepted that the medical personnel of the fighting armies should be retained by the detaining powers, as needed for the prisoners. Such personnel would be given any benefits due prisoners of war. The principle of captivity of medical personnel was then voted for. Several delegations, however, while recognizing the humanitarian thoughts

behind the Anglo-Saxon request, became alarmed at the possible consequences of this new principle and decided to attempt to restore the original principle of noncaptivity. Since then there have been these two contradictory principles, and their supporters have not ceased their opposition.

In Stockholm in 1948, at the preliminary Conference of the Red Cross, which established the basis of the discussions of the Diplomatic Conference of Geneva, the principle of noncaptivity of medical and religious personnel was voted for by an imposing majority.

At Geneva in 1949, to avoid reopening the debate, the majority of the delegates were ready to maintain the text of Stockholm. However, the delegation of the United Kingdom presented an amendment which called for separation of captured medical personnel from the convention concerning the injured and sick and insertion in the convention on the treatment of prisoners. A formula of agreement finally was worked out and adopted.

Insignia of the Red Cross

With respect to the insignia of protection, there is now a tendency to abandon the use of the Red Cross and to adopt a universal sign, a simple geometric figure which has no political or religious significance in any part of the world. This is, however, still controversial. The diversity of signs employed at present can only be a weakening element. In addition to the sign of the Red Cross, there exists the crescent, the sun and the red lion, and recently Israel has asked recognition for the red shield of David.

International Medical Code

The idea that medicine of the entire world should be regulated by an international medical code, like that which has been proposed by the Medico-Juridical Commission of Monaco, is becoming better crystallized. Under the auspices of the Sovereign Prince of Monaco a collective work is being published, which is the first attempt at codification of international medical law, as has already been advocated by the World Medical Association.

TURKEY

(From Our Regular Correspondent)

ANKARA, Aug. 22, 1949.

Streptomycin Therapy in Tuberculosis

Twenty-three years ago the Ministry of Public Instructions established in Istanbul a 300 bed preventorium and a 200 bed sanatorium for the free treatment of pretuberculous students and tuberculous teachers and students. The ministry appoints the physicians and other employees. Dr. Zeki Köseoglu, chief physician, and Dr. N. Pinar reported on the use of streptomycin in 88 of these patients, of whom 74 had pulmonary tuberculosis and 14 tuberculosis of other organs. Forty-six patients were at first given a daily dose of 2 Gm. of streptomycin, which was later reduced to 1.5 Gm. (one injection every six hours). Four patients received a daily dose of 1 Gm. (one injection every twelve hours). The average total amount given was 119 Gm.; the average time of treatment was sixty-four days. Excellent results were obtained in 7 patients with acute and subacute pulmonary and miliary tuberculosis. Five of these patients recovered completely; all clinical symptoms disappeared, and results of radiographic examinations were negative. At the end of the treatment the sputum of all patients was negative on concentration and culture. Of 27 patients with exudative and exudative-productive tuberculous infiltration, 4 recovered completely, 15 showed decided improvement and 8 only slight improvement. The sputum was normal in 84 per cent of these patients.

Of 40 patients with chronic fibroid and fibroid-caseous tuberculosis, amelioration was moderate in 12 and only slight in a few. Four patients died while receiving treatment. In 5 of 7 patients with simple thin-walled cavities, the cavities closed and decreased in size, and in 1 patient the cavity remained unchanged. In 3 patients with ascitic tuberculous peritonitis, excellent results were obtained, absorption of exudate occurred within a few weeks. Streptomycin therapy was satisfactory in 5 patients with tuberculous laryngitis associated with moderate or far advanced pulmonary tuberculosis. Of 3 patients with tuberculous meningitis, streptomycin therapy failed in 2 patients, and 1 patient recovered. Streptomycin did not have any beneficial effect on 3 patients with tuberculous empyema.

These results indicate that streptomycin promises to be a powerful chemotherapeutic agent for pulmonary tuberculosis but that at present streptomycin therapy should not be regarded as a substitute for other methods but as complementary to them. Streptomycin is indicated for the treatment of miliary and hematogenous disseminated nodular tuberculosis, especially exudative infiltration, acute bronchopneumonic tuberculosis and other bronchogenic diffusions. Streptomycin is also effective in the treatment of tuberculous lesions of mucous membranes and tuberculous meningitis. It can be used intermittently in small doses for symptomatic relief in chronic types of tuberculosis.

New Maternity Hospital

The first maternity hospital in Ankara was established by the Ministry of Health and Social Assistance in 1924. Ankara then had a population of 71,425. The maternity had 10 beds and was housed in an old two story frame building. Applications for admission chiefly came from wives of civil servants and school teachers; the natives almost never sought admission. As a means of filling the often vacant beds, the obstetricians and midwives in charge resorted to personally conducted propaganda, drawing the attention of pregnant native women to the maternity hospital, by showing them round the hospital and by explaining that all care and attendance was free of charge. As time went on more and more native women came to the hospital, so that 15 more beds were soon added and there was still a waiting list. Then the maternity hospital was moved to a three story concrete building. During the last ten years it often happened that in a single day there were as many as twenty deliveries, including cases of abnormal conditions and ectopic pregnancies.

Though the foundation stone of the new 200 bed Ankara Maternity Hospital was laid in 1937, the lack of building material and equipment and the inflation during the second World War prevented the hospital's being ready to receive patients until the beginning of 1949. The more than 135 free beds were soon occupied. The five story building in the center of the city has all modern conveniences, private rooms and nurseries.

The Ankara Maternity Hospital has from its inception in 1924 been under the direction of chief obstetrician and gynecologist Dr. Zekai Tahir Burak.

There are at present twenty-four obstetricians and interns and twenty midwives, and plans for a school for midwives and nurses to be trained at the maternity hospital are under way. The maternity is attached to the Ministry of Health and Social Assistance and is entirely supported from its funds.

According to the 1945 census the 26 year old capital of the Turkish Republic had a population of 227,506, which is continually increasing. Other institutions with obstetric departments are the University Gülhane Hospital, the government railway hospital, the municipal hospital and the military hospital, with a total of nearly 300 beds. There are two busy private maternity hospitals in Ankara.

There are at present forty-one obstetricians, including interns, in Ankara; of these, six are women. Seventy per cent of all deliveries are still attended by midwives in the homes. The maternal mortality rate at the maternity hospital is 2.6 per thousand as against 5.3 formerly, when patients from outlying

rural communities arrived in an advanced critical stage. There are no quintuplets or quadruplets in the twenty-four year record of the maternity hospital, but 4 per cent were twins; triplets were rare.

The birth rate of Ankara is 20 to 25 per thousand. Two-thirds of the population consists of civil servants, teachers, school children and university students. The birth rate in rural communities is 35 to 40 per thousand. The 1929 Public Health Law prohibits birth control in Turkey.

Correspondence

MORE BEDS FOR THE TUBERCULOUS

To the Editor:—It seems to me there is one important point overlooked in the editorial in THE JOURNAL, August 20, on "The Demand for More Beds for the Tuberculous." The cost of the additional beds needed now for tuberculous patients can be justified when they are added to regional general hospitals. Tuberculosis in many sections of the country is disappearing rather rapidly. The national decline in the death rate of 11 per cent last year was an acceleration of the decline that has been going on for the past forty years. As the disease is discovered in its earlier stages, it is becoming more and more a general hospital problem like any other acute illness. The beds, when they are constructed in general hospitals, can be used for other types of patients when tuberculosis disappears. There is a possibility, perhaps even a probability, that medical science will find a specific cure for tuberculosis that will make it as rare as typhoid within a short time.

GRAHAM L. DAVIS, Battle Creek, Mich.

INDUSTRIAL POLLUTION OF ENVIRONMENT

To the Editor:—The editorial "Industrial Pollution of Human Environment," in THE JOURNAL, Aug. 27, 1949, is of vital interest to me and should be to every person concerned in national health. From 1903 to 1913 I was engaged in the practice of industrial medicine and surgery in the Pittsburgh area. As chief surgeon to several large industrial concerns it was my duty to conserve as many working days as possible for employees. In the years 1903 to 1908 the mortality rate from typhoid ranged from 150 to 180 per 100,000; the morbidity rate was alarming. Investigation of the source of infection revealed pollution of all water supplies. Where political bosses' contractors were supposed to be supplying the city with water from the Aspinwall filtration plant, the city was getting only 50 per cent potable water. To obviate this, the Brilliant pumping station source of supply was pumping sewage water into the Highland Park reservoir. The result of this investigation was given to the Pittsburgh papers. I then wrote an article, "The Responsibilities of Municipalities in the Ohio Valley for Epidemics of Typhoid" (J. A. M. A. **51**: 1496 [Oct. 31] 1908) which was followed by action of the municipalities and eventually resulted in a pure water supply for Pittsburgh and other cities. This, however, did not solve the sanitary problem.

After this, I called attention to insect carriers of disease (Blue-Bottle Flies as Carriers of Infection, J. A. M. A. **53**: 1561 [Nov. 6] 1909; Insect Carriers of Typhoid, J. A. M. A. **57**: 1432 [Sept. 3] 1912), and then the industrial hazard (Vanadiumism, J. A. M. A. **56**: 1648 [June 3] 1911). After my article "Laws Relative to the Sanitary Control of Public Eating and Drinking Places" (J. A. M. A. **59**: 2020 [Dec. 7] 1912) the commissioner of health of the Commonwealth of Pennsylvania, Dr. Dixon, initiated the enactment of laws which went far to correct this sanitary problem and was followed by similar legislation in other states. At this time, some forty years later, these attempts to set forth the type and degree of health hazards may appear feeble, but at least it was a beginning of a more healthful era.

The editorial is a succinct statement of facts. What are state and federal governments doing to remedy conditions hazardous to human life? If they now disregard the lives of the American people, what are they going to do under socialized medicine? Socialized medicine, as observed at work in Europe, has made sick beggars of its people. If Americans want to be treated like the *verdammte schweinhund,* they should support the proposed laws of the welfare state.

The administration can contribute billions for the preservation of political security but only scant millions for the health of the American people. If it were not for the unselfish work of physicians and lay foundations for the investigation of health problems, the health of our people would be at an all-time low. As matters stand today, the United States is the healthiest nation on earth. When the mortality and morbidity from cardiovascular diseases, cancer, poliomyelitis and industrial diseases are increasing at an alarming rate, such a condition should stimulate thinking physicians and laymen to action on the subject of industrial pollution of human environment.

W. FOREST DUTTON, M.D., Noel, Mo.

REFRIGERATION ANESTHESIA

To the Editor:—In further reply to Dr. de Takat's letter on this subject (THE JOURNAL, July 16, 1949, page 974):

1. His original statement which prompted my criticism, namely, that all refrigerated tissues must be amputated, is obviously untrue, as proved by hundreds of successfully healed amputations after refrigeration anesthesia.

2. Tourniquet paralysis has nothing to do with this statement. It is not a problem in the amputations for which refrigeration has been chiefly used. There are ways of avoiding it for orthopedic or other operations.

3. Large and Heinbecker's repetition of the long familiar production of "immersion foot" damage by ninety-six hours of continuous soaking in ice water has already been fully answered (*Arch. Phys. Med.* **26**:92-98, 1945). This being their argument against brief refrigeration anesthesia, I invited them to keep up any of their preferred forms of anesthesia for ninety-six hours continuously and compare results. Furthermore, Dr. de Takats should notice that even after this ninety-six hour mistreatment the legs did not require amputation.

4. It is surgically false that wrapping limbs in cotton and maintaining normal body temperature will prevent gangrene after iliac or femoral artery occlusion. Refrigeration was the essential factor in preservation by Mock and others whom I cited.

5. Evidently there is still a lack of comprehension of the distinction between effects of temperature and effects of defense reactions (*Canad. M. A. J.* **51**:220-226, 1944; *Anesth. & Analg.* **24**:51-65, 1945; *Clinics* **4**:1642-1674, 1946). The best preservation by cold is illustrated in reactionless isolated tissues (grafts, thrombotic or amputated limbs). Especially the limbs with circulation react with the "immersion foot" changes and require judgment of emergencies which demand radical refrigeration and other occasions for milder cooling, as illustrated in Kross's eleven week treatment of a burned leg (J. A. M. A. **128**:19-20 [May 5] 1945; *S. Clin. North America* **25**:361-370, 1945; *Arch. Surg.* **49**:12-22 [July] 1944). Every form of therapy is supposed to be guided by skill and experience, and disregard of this requirement in the use of hypothermia is responsible for the attacks on it.

FREDERICK M. ALLEN, M.D., New York.

Bureau of Legal Medicine and Legislation

MEDICOLEGAL ABSTRACTS

Charitable Hospitals: Extent of Tax Exemption. — A number of California hospitals filed separate suits to recover taxes which they contended were wrongfully collected because of their tax-exempt status. All of the suits were consolidated for trial, and, after a hearing in the superior court, the various parties appealed and cross appealed to the district court of appeals, second district, division 1, California.

At the general election held Nov. 7, 1944, an amendment to the California constitution was approved which provided: "In addition to such exemptions as are now provided in this Constitution, the Legislature may exempt from taxation all or any portion of property used exclusively for religious, hospital or charitable purposes and owned by community chests, funds, foundations or corporations organized and operated for religious, hospital or charitable purposes, not conducted for profit and no part of the net earnings of which inures to the benefit of any private shareholder or individual." The following year the legislature, under the permission granted it by the foregoing constitutional amendment, enacted Section 214 of the Revenue and Taxation Code, which exempted "Property used exclusively for religious, hospital, scientific or charitable purposes owned and operated by community chests, funds, foundations or corporations organized and operated for religious, hospital, scientific or charitable purposes . . ." under certain conditions.

A reasonable construction of the "welfare exemption," said the court of appeal, is grounded on sound legal principles. The existence in a community of a hospital which admits, cares for and gives medical aid to the sick and afflicted whether rich or poor, not without compensation in all cases but where in all cases, any fees collected go to pay the expense of operation of the hospital and not to the profit of the founders or shareholders is a public charity in the fullest sense. The policy of tax exemption of hospitals is not founded on maudlin sentiment but on a sound economic principle that the benefits derived by the community at large from the services rendered by such institutions far outweigh the trivial inequality caused by an exemption of their property from taxes. Their ultimate contribution to the public good returns more than a fair equivalent for the exemption afforded them. A "hospital" is primarily a service organization. It furnishes a place where the patient, whether poor or rich, can be treated under ideal conditions. It makes available room, special diet, x-ray, laboratory, surgery and a multitude of other services and equipment now available through the advances of medical science. These facilities also stand ready to serve the community in times of epidemic or disaster. As to what is meant by the phrase "hospital purpose," said the court, we are persuaded that it embraces those facilities or services that must be regarded as reasonable, necessary or appropriate to accomplish the functions of a hospital in furnishing a complete and efficient hospital service to its patients, its doctors and its community.

The first question presented by the appeal, said the court, is whether the use of property by plaintiff hospitals for a nurses' training school and to provide housing for hospital interns, residents, student nurses and other alleged essential employees required to be readily available, constitutes a use exclusively for hospital purposes and therefore renders the property exempt under the welfare exemption. In order to be "used exclusively," as contemplated by the statute, the use must be essential to the operation and conduct of the hospital. If the major hospitals did not operate nursing schools, no student nurses would be available and resort would have to be made to registered nurses at a much greater expense to patients. And obviously, if hospitals did not train nurses, eventually there would be no registered nurses available. It is a matter of common knowledge that in many if not in most hospitals, nurses and student nurses sleep in the hospital building or in a building adjoining the hospital. Manifestly, an emergency condition may arise from time to time during the night requiring immediate attention, which makes it necessary to have more nursing personnel available than is actually on night time duty. This can be accomplished, as alleged by the plaintiffs, only by furnishing housing facilities on the hospital grounds for nurses, student nurses and kindred aids. In so far as the exemption of property used to provide housing for interns, superintendents and other employees is concerned, it will suffice to say that the administration of the affairs of the institution requires that certain personnel and employees be located on the property to the end that the operation may be efficiently conducted and supervised and that emergency cases be cared for as they arise. It is commonly and generally known that admittance may be gained to a hospital at any hour of the day or night. To supply such service, help obviously must be on hand to provide for the handling of such emergencies. We entertain no doubt, the court concluded, that the term "property used exclusively for . . . hospital . . . purposes" means not only the buildings and grounds actually used for housing patients, but adjacent buildings and grounds which are reasonably necessary or appropriate to the purposes and objects of the hospital and which are used directly for the promotion and accomplishment of the same.

The next question was whether buildings under construction, intended to be for use exclusively for hospital purposes and later so used, were within the welfare exemption. The trial court concluded that the welfare tax exemption did not apply to property on which buildings were under construction, even though such buildings were designed and intended exclusively for a hospital or for other hospital purposes. We are persuaded, said the court of appeals, that under a reasonable interpretation the property under consideration should be considered as "used exclusively" for hospital purposes. The rule is epitomized in a Pennsylvania case which said, "Would anyone contend that, if a hospital burned to the ground, that the ground on which a new structure was being built and the incompleted building itself, would be subject to taxation? We see no difference in principle between such a case and the one before us. It cannot be said that the ground and the partly erected building thereon is not a part of the hospital merely because the operations of the hospital are excluded from it while the building is in course of erection. . . ."

The next question was whether property used to furnish limited recreational facilities to student nurses, interns and residents was entitled to exemption. The property consists of a tennis court located on the hospital grounds, used as an outdoor recreational facility for the student nurses, interns and residents. The court said that there is no denial of the fact that the nature and type of the recreational facility here under consideration is of a reasonable character both as to the relationship of its cost and size and location of the hospital. It is as important to conserve the health of the nurses, student nurses, interns and residents of the hospital as it is to restore the health of its patients, because on the existence of the former depends to a large extent the accomplishment of the latter.

Finally, the question was raised as to whether hospital property used to house a "thrift shop" in conjunction with the charitable activities of such hospital was entitled to exemption. The "thrift shop" is located in a portion of one of the plaintiff hospital buildings. Donated clothing and furnishings were sold by the Women's Auxiliary of the California Babies' and Children's Hospital, an authorized agency of the Los Angeles Community Chest, and the entire proceeds of the shop were devoted to the maintenance of the free children's clinic maintained jointly by the plaintiff and the agency. We are convinced, said the court of appeals, that the property on which the thrift shop was conducted was exclusively used for hospital and purely charitable purposes. This is not a commercial enterprise and does not compete with tax-paying business. The property is used for the purpose of receiving and converting gifts of clothing and furnishings into cash to assist in financing a free clinic for children—strictly a hospital purpose. The thrift shop is not operated for a "profit" as is generally the primary purpose of business. The primary purpose of the thrift shop, on the contrary, is to aid sick and afflicted children by maintaining for their benefit a free clinic. It operates only to convert the

gifts of personal property into cash to be used in maintaining a free clinic for children—purely a hospital purpose.

Accordingly it was held that a charitable hospital does not lose its tax exemption when it makes use of its property for the purpose of providing housing for the hospital interns, student nurses and other essential employees, for a training school for its student nurses, for furnishing recreational facilities for its student nurses, interns and residents, or for using its property to house a thrift shop in conjunction with its charitable activities, nor did the hospital property on which buildings were under construction lose its taxation-exempt status.—*Cedars of Lebanon Hospital v. Los Angeles County et al. (5 cases), 206 P. (2d) 915 (Calif., 1949).*

Medical Examinations and Licensure

COMING EXAMINATIONS AND MEETINGS

NATIONAL BOARD OF MEDICAL EXAMINERS

NATIONAL BOARD OF MEDICAL EXAMINERS. *Parts I and II,* Feb. 13-15. Centers where there are approved medical schools and five or more candidates. Exec. Sec., Mr. E. S. Elwood, 225 S. 15th Street, Philadelphia 2.

EXAMINING BOARDS IN SPECIALTIES

AMERICAN BOARD OF ANESTHESIOLOGY, INC. *Oral.* Denver, Oct. 16-20 Sec., Dr. Curtiss B. Hickcox, 745 Fifth Ave., New York 27.

AMERICAN BOARD OF DERMATOLOGY AND SYPHILOLOGY, INC.: *Oral.* Cincinnati, Oct. 21-23. Sec., Dr. George M. Lewis, 66 East 66th St., New York 21.

AMERICAN BOARD OF INTERNAL MEDICINE: *Written.* Oct. 17. Asst. Sec.-Treas. Dr. W. A. Werrell, 1 Main St., Madison 3, Wis.

AMERICAN BOARD OF NEUROLOGICAL SURGERY: *Oral.* Chicago, June 3. Final date for filing applications is Jan. 1. Sec., Dr. W. J. German, 789 Howard Ave., New Haven.

AMERICAN BOARD OF OBSTETRICS AND GYNECOLOGY, INC. *Part I.* Various Centers. Feb. 3. Final date for filing application is Nov. 5. Sec., Dr. Paul Titus, 1015 Highland Bldg., Pittsburgh.

AMERICAN BOARD OF OPHTHALMOLOGY: St. Louis, Oct. 15-19; Boston, April. Sec., Dr. Edwin B. Dunphy, 56 Ivie Rd., Cape Cottage, Maine.

AMERICAN BOARD OF ORTHOPAEDIC SURGERY. *Part II,* New York City, Feb. 9-10. Sec. Treas., Dr. Harold A. Sofield, Room 1856, 122 S. Michigan Ave., Chicago.

AMERICAN BOARD OF OTOLARYNGOLOGY: Chicago, Oct. 4-7. Sec., Dr. D. M. Lierle, University Hospitals, Iowa City.

AMERICAN BOARD OF PATHOLOGY: Chicago, Oct. 7-8. Sec., Dr. Robert A. Moore, 507 Euclid Ave., St. Louis.

AMERICAN BOARD OF PEDIATRICS: New York City, Oct. 21-23; Chicago, Dec. 9-11. Sec., Dr. John McK. Mitchell, 6 Cushman Road, Rosemont, Pa.

AMERICAN BOARD OF PLASTIC SURGERY: Examinations are given in June and November of each year in the home town of applicants. Sec.-Treas., Dr. Louis T. Byars, 400 Metropolitan Bldg., St. Louis, Mo.

AMERICAN BOARD OF PREVENTIVE MEDICINE AND PUBLIC HEALTH: *Parts I and II.* New York, Oct. 22-24. Sec., Dr. Ernest L. Stebbins, 615 N. Wolfe St., Baltimore.

AMERICAN BOARD OF PROCTOLOGY: November. Sec., Dr. Louis A. Buie, 102-110 Second Ave., S.W., Rochester, Minn.

AMERICAN BOARD OF PSYCHIATRY AND NEUROLOGY, INC. *Special Examination.* Chicago, Oct. 24-25. December, New York City. Sec., Dr. F. J. Braceland, 102-110 Second Ave., S.W., Rochester, Minn.

AMERICAN BOARD OF SURGERY: *Written.* Various Centers, October 26. Sec., Dr. J. Stewart Rodman, 225 S. 15th St., Philadelphia.

AMERICAN BOARD OF UROLOGY: *Written.* December. *Oral and Clinical.* Chicago, Feb. 11-15. Sec., Dr. Harry Culver, 7935 Sunnyside Road, Minneapolis 18.

BOARDS OF MEDICAL EXAMINERS

ALABAMA: *Examination.* Montgomery, June 27-29. Sec., Dr. D. G. Gill, 519 Dexter Avenue, Montgomery.

ARKANSAS: * *Examination.* Little Rock, Nov. 3-4. Sec., Dr. Joe Verser, Harrisburg. *Eclectic.* Little Rock, Nov. 3. Sec., Dr. Clarence H. Young, 1415 Main St., Little Rock.

COLORADO: * *Endorsement.* Denver, Oct. 4. Sec., Dr. George H. Gillen, 831 Republic Building, Denver.

CONNECTICUT: * *Examination.* Hartford, Nov. 8-9. Secretary to the Board, Dr. Creighton Barker, 160 St. Ronan Street, New Haven.

DELAWARE: *Examination.* Dover, Jan. 10-12. *Reciprocity.* Dover, Jan. 19. Sec., Dr. J. S. McDaniel, 229 State Street, Dover.

DISTRICT OF COLUMBIA: * *Examination.* Washington, Nov. 14-15. Sec., Dr. G. C. Ruhland, 4130 E. Municipal Bldg., Washington.

FLORIDA: * *Examination.* Jacksonville, Nov. 27-29. Sec., Dr. Frank D. Gray, 12 N. Rosalind Ave., Orlando.

GEORGIA: *Examination.* Atlanta, Oct. 11-12. *Reciprocity.* Atlanta, Oct. 13. Sec., Mr. R. C. Coleman, 111 State Capitol, Atlanta 3.

GUAM: *Endorsement.* Agana, Last Friday of each month. Sec., Capt. C. K. Youngkin, Dept. of Public Health, Guam, % F.P.O., San Francisco.

IDAHO: Boise, Jan. 9. Exec. Sec., Mr. Armand L. Bird, 305 Sun Building, Boise.

ILLINOIS: Chicago, Oct. 4-6. Supt. of Registration, Mr. Fred W. Rueve, Capitol Bldg., Springfield.

INDIANA: *Examination.* Indianapolis, June. Sec., Dr. Paul R. Tindall, 1138 K. of P. Bldg., Indianapolis.

IOWA: * *Examination.* Des Moines, Dec. 5-7. *Reciprocity.* Des Moines, Oct. 3, Nov. 7, Dec. 5. Sec., Dr. M. A. Royal, 506 Fleming Bldg., Des Moines.

KANSAS: Topeka, Dec. 8-9. Sec., Dr. J. F. Hassig, 905 N. Seventh St., Kansas City.

KENTUCKY: Louisville, Dec. 12-14. Sec., Dr. Bruce Underwood, 620 South Third Street, Louisville 2.

LOUISIANA: New Orleans, December. Sec., Dr. Roy B. Harrison, 1507 Hibernia Bank Building, New Orleans 12.

MAINE: Portland, Nov. 8-9. Sec., Dr. Adam P. Leighton, 192 State Street, Portland.

MARYLAND: *Examination.* Baltimore, Dec. 13-16. Sec., Dr. Lewis P. Gundry, 1215 Cathedral St., Baltimore 1. *Homeopathic. Examination.* Baltimore, Dec. 13-14. Sec., Dr. John A. Evans, 612 West 40th St., Baltimore.

MASSACHUSETTS: Boston, Nov. 15-18. Sec., Dr. George L. Schadt, 413 East State House, Boston.

MICHIGAN: * *Examination.* Lansing, Oct. 12-14. *Reciprocity.* Oct. 11. Sec., Dr. J. Earl McIntyre, 100 W. Allegan Street, Lansing 8.

MINNESOTA: * Oct. 18-19. Sec., Dr. Julian F. Du Bois, 230 Lowry Medical Arts Bldg., St. Paul 2.

MISSISSIPPI: *Reciprocity.* Jackson, December. Sec., Dr. Felix J. Underwood, State Board of Health, Jackson 113.

MISSOURI: *Examination.* Jefferson City, October 24-26. *Reciprocity.* Kansas City, October, 23. Exec. Sec., Mr. John A. Hailey, State Capitol Building, Jefferson City.

MONTANA: Helena, Oct. 3-5. Sec., Dr. Otto G. Klein, First National Bank Bldg., Helena.

NEVADA: Carson City, Nov. 7. Sec., Dr. George H. Ross, 112 N. Curry St., Carson City.

NEW JERSEY: Oct. 18-21. Sec., Dr. E. S. Hallinger, 28 W. State St., Trenton.

NEW MEXICO: * Santa Fe, Oct. 10-11. Sec., Dr. Charles J. McGoey, Coronado Bldg., Santa Fe.

NEW YORK: *Examination.* New York, Albany, Syracuse and Buffalo, Oct. 4-7. Sec., Dr. Jacob L. Lochner Jr., 23 S. Pearl St., Albany 7.

NORTH CAROLINA: *Endorsement.* Asheville, Oct. 17. Sec., Dr. Ivan Proctor, 226 Hillsboro Street, Raleigh.

NORTH DAKOTA: *Examination.* Grand Forks, Jan. 4-6. *Reciprocity.* Jan. 7. Sec., Dr. C. J. Glaspel, Grafton.

OHIO: *Examination.* Columbus, December. *Endorsement.* Oct. 2. Sec., Dr. H. M. Platter, 21 W. Broad St., Columbus.

OKLAHOMA: * *Examination.* Oklahoma City, June 7-8. Sec., Dr. Clinton Gallaher, 813 Braniff Building, Oklahoma City.

OREGON: * *Endorsement.* Portland, Nov. 4-9. Exec. Sec., Mr. Howard I. Bobbitt, 608 Failing Building, Portland.

PENNSYLVANIA: *Examination.* Philadelphia or Harrisburg, January. Acting Sec., Mrs. Marguerite G. Steiner, 351 Education Building, Harrisburg.

RHODE ISLAND: * *Examination.* Providence, Oct. 6-7. Chief, Mr. Thomas B. Casey, 366 State Office Building, Providence.

SOUTH CAROLINA: *Examination.* Columbia, Nov. 8-9. *Reciprocity.* First Monday of every month. Sec., Dr. N. B. Heyward, 1329 Blanding St., Columbia.

SOUTH DAKOTA: * Sioux Falls, Jan. 17. Sec., Dr. C. E. Sherwood, 300 First National Bank Building, Sioux Falls.

VIRGINIA: *Examination.* Richmond, Dec. 2-3. *Reciprocity.* Richmond, Dec. 1. Sec., Dr. K. D. Graves, 631 First St., S.W., Roanoke.

WASHINGTON: * Seattle, January. Director, Department of Licenses, Mr. Edward C. Dohm, Olympia.

WEST VIRGINIA: *Examination.* Charleston, Oct. 3-5. *Reciprocity.* Charleston, Oct. 3. Director, State Health Department, Dr. N. H. Dyer, Room 639, Capitol Building, Charleston.

WISCONSIN: * *Examination.* Madison, Jan. 10-12. Sec., Dr. C. A. Dawson, River Falls.

WYOMING: Cheyenne, Oct. 3. Sec., Dr. Franklin D. Yoder, Capitol Bldg., Cheyenne.

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* Basic Science Certificate required.

BOARDS OF EXAMINERS IN THE BASIC SCIENCES

ARKANSAS: *Examination.* Little Rock, Oct. 4. Sec., Mr. L. E. Gebauer, 1002 Donaghey Bldg., Little Rock.

CONNECTICUT: New Haven, Oct. 8. Executive Assistant, State Board of Healing Arts, Miss Mary G. Reynolds, 110 Whitney Ave., New Haven 10.

DISTRICT OF COLUMBIA: Washington, Oct. 24-25. Sec., Dr. G. C. Ruhland, 4130 E. Municipal Bldg., Washington.

FLORIDA: *Examination.* Gainesville, Nov. 5. Sec., Mr. M. W. Emmel, University of Florida, Gainesville.

IOWA: *Examination.* Des Moines, Oct. 11. Sec., Dr. Ben H. Peterson, Coe College, Cedar Rapids.

MICHIGAN: *Examination.* Detroit and Ann Arbor, Oct. 14-15. Sec., Miss Eloise LeBeau, 101 N. Walnut St., Lansing 15.

MINNESOTA: *Examination.* Minneapolis, Oct. 4-5. Sec., Dr. Raymond N. Bieter, 105 Millard Hall, University of Minnesota, Minneapolis.

NEBRASKA: *Examination.* Omaha, Oct. 4-5. Director, Bureau of Examining Boards, Mr. Oscar F. Humble, Room 1009, State Capitol Bldg., Lincoln 9.

OKLAHOMA: *Examination.* Oklahoma City, April 11. Sec., Dr. Clinton Gallaher, 813 Braniff Building, Oklahoma City.

OREGON: Portland, Dec. 3. Sec., Mr. Charles D. Byrne, State Board of Higher Education, Eugene.

SOUTH DAKOTA: Vermillion, Dec. 2-3. Sec., Dr. Gregg M. Evans, 310 E. 15th St., Yankton.

WASHINGTON: Seattle, January. Director, Department of Licenses, Mr. Edward C. Dohm, Olympia.

WISCONSIN: Milwaukee, Dec. 3. Sec., Prof. W. H. Barber, Ripon College, Ripon.

Current Medical Literature

AMERICAN

The Association library lends periodicals to members of the Association and to individual subscribers in continental United States and Canada for a period of three days. Three journals may be borrowed at a time. Periodicals are available from 1938 to date. Requests for issues of earlier date cannot be filled. Requests should be accompanied by stamps to cover postage (6 cents if one and 18 cents if three periodicals are requested). Periodicals published by the American Medical Association are not available for lending but can be supplied on purchase order. Reprints as a rule are the property of authors and can be obtained for permanent possession only from them.

Titles marked with an asterisk (*) are abstracted below.

American Heart Journal, St. Louis

37:689-848 (April 15) 1949

*Effect of Low Fat Diet on Spontaneously Occurring Arteriosclerosis of Chicken. L. Horlick, L. N. Katz and J. Stamler.—p. 689.

*Anticoagulation Therapy with Heparin/Pitkin Menstruum in Management of Coronary Artery Thrombosis and Its Complications. L. Loewe and H. B. Eiber.—p. 701.

IV. Correlation of Electrocardiographic and Pathologic Findings in Infarction of Interventricular Septum and Right Ventricle. G. B. Myers, H. A. Klein and T. Hiratzka.—p. 720.

Method for Recording Arterial Pressure Pulse and Blood Pressure in Man. L. H. Peterson, R. D. Dripps and G. C. Risman.—p. 771.

New Capacitance-Blood-Pressure-Manometer Amplifier. H. E. Tompkins.—p. 783.

Electrocardiographic Changes Following Electroshock Therapy in Curarized Patients. M. R. Hejtmancik, A. J. Bankhead and G. R. Herrmann.—p. 790.

Measurement of QRS Complex and Interpretation Thereof by Direct and Indirect Deduction. J. B. Kleyn and R. M. F. Houtappel.—p. 806.

Low Fat Diet in Pathogenesis of Arteriosclerosis in Chickens.—Horlick and co-workers fed one group of 16 chickens unlimited quantities of chick starter mash and water. A second group of 14 chickens of the same age received the same chick starter mash from which the fat and cholesterol had been largely removed by alcohol-ether extraction. This diet was made isocaloric by the addition of sucrose, and the vitamins removed in the extraction process were replaced. Feeding was continued for sixty-three weeks. Gross atherosclerosis was observed in 5 chickens (35 per cent) on the low fat diet and in 10 chickens (63 per cent) on the control diet. The lesions appeared earlier and were severer in the control group. The incidence of microscopically visible lesions was equal in both groups. There was no essential difference in the structure of the lesions. The low fat group showed blood cholesterol levels which were consistently higher than those of the control group throughout the course of the experiment. Lipid analysis of the blood at the conclusion of the experiment revealed that all the lipid fractions of the blood were slightly higher in the low fat group than in the control group. It would seem that the evidence does not warrant wholesale restriction of lipids in attempts to prevent the onset of arteriosclerosis. There is suggestive evidence that fat restriction may be a judicious measure in patients with hypercholesteremia even of a moderate degree and possibly in patients with a bad family history of coronary or cerebral arteriosclerosis.

Anticoagulation Therapy with Heparin/Pitkin Menstruum.—Loewe and Eiber treated 20 consecutive, unselected patients, 15 men and 5 women between the ages of 35 and 76, who had acute coronary artery thrombosis and myocardial infarction with heparin in the Pitkin menstruum. The initial dose was 400 mg. administered subcutaneously in the usual manner. Repetitive doses of 400 mg. were generally given every other day during the acute thrombotic phase in order to prevent propagation and to promote resolution of the thrombus. This schedule should be maintained for three to four doses to achieve a continuous and adequate heparin response. Thereafter, if justified by the anticoagulation effects, the individual dose may be given at longer intervals and the amount of the drug per dose reduced to 300 mg. or even 200 mg., as dictated by the specific case. The total dose varied from 1,200 to 3,350 mg. All of the patients in this series were seriously ill, and some were desperately ill. Fourteen of the patients had clinically detectable, complicating thromboembolic episodes. One of these complicated cases was fatal and represented the only treatment failure in the entire series. In none of the 19 patients who recovered was there evidence of thrombus propagation, once anticoagulation therapy was instituted. All complicating thromboembolic processes were promptly terminated. In the optimally treated patients the span of bed rest was conspicuously reduced. Convalescence was accelerated, and the patients were restored more rapidly to their accustomed activity. The gratifying response of this small though representative series of gravely ill patients seems to indicate that heparin in a Pitkin menstruum, because of the simplicity of administration, prompt effectiveness and absence of toxicity, is well suited for the treatment of acute coronary artery thrombosis and its complications.

American Journal of Diseases of Children, Chicago

76:365-484 (Oct.) 1948

Humanizing Hospital Experiences: Presidential Address. G. F. Powers.—p. 365.

*Occurrence of Complications in Scarlet Fever Treated with Penicillin, Antitoxin and Gamma Globulin. J. F. Landon and N. Greenfield.—p. 380.

Salmonella Derby Meningitis: Report of Case of Two Month Old Infant. K. Schweig, F. C. Green and A. Nathan.—p. 384.

Toe Reflexes in Infancy and Development of Voluntary Control. E. F. Gentry and C. A. Aldrich.—p. 389.

Studies on Relation of Hemolytic Streptococcus to Rheumatic Fever: I. Review of Serologic Literature. T. N. Harris.—p. 411.

Scarlet Fever.—Landon and Greenfield treated 245 patients with scarlet fever with penicillin, gamma globulin and scarlet fever Streptococcus antitoxin U. S. P. in rotation. There were three and one-half times as many complications in the group treated with penicillin as in the group receiving gamma globulin and five times as many complications in the group treated with antitoxin as in the group receiving gamma globulin. There were over twice as many severely ill patients in those treated with antitoxin as in those receiving penicillin and over three times as many as in the group receiving gamma globulin. In patients in whom complications developed there was no indication of any relation to the severity of the disease. The percentage of throat cultures showing hemolytic streptococci at discharge in the group treated with gamma globulin was 82 per cent, in the group treated with penicillin 54 per cent and in the group receiving antitoxin 35 per cent, thus suggesting the ineffectiveness of gamma globulin in clearing the throat of hemolytic streptococci. The comparison of the three agents reveals that gamma globulin is the most effective in reducing the number of early and late complications in scarlet fever, despite the fact that it is relatively ineffective in clearing the throat of the hemolytic streptococci as compared with the other two agents. This work tends to confirm the observations of a previous study.

American Journal of Medicine, New York

6:405-534 (April) 1949

*Aureomycin in Typhus and Brucellosis. V. Knight, F. Ruiz-Sanchez, A. Ruiz-Sanchez and W. McDermott.—p. 407.

Effect of Streptomycin Therapy on Bacterial Flora of Throat. C. P. Miller and M. Bohnhoff.—p. 417.

Immunization of Human Beings with Group A Hemolytic Streptococci. L. A. Rantz, E. Randall and H. H. Rantz.—p. 424.

*Treatment of Acute Rheumatic Fever with Aspirin with Special Reference to Biochemical Changes. W. S. Hoffman, M. Pomeranz, I. F. Volini and C. Nobe.—p. 433.

Relative Infectivity of Blood and Cerebrospinal Fluid in Secondary Syphilis. C. N. Frazier and H. C. Pian.—p. 443.

Penicillin in Oil and Beeswax in Treatment of Syphilis in Clinic Patients. H. Eisenberg and F. Plotke.—p. 449.

Auricular Flutter in Association with Myocardial Infarction: Its Prognosis and Management. J. M. Askey.—p. 453.

Role of Tonsillectomy in Management of Recurrent Streptococcal Sore Throat, Rheumatic Fever and Glomerulonephritis. M. Michael Jr.—p. 462.

Aureomycin in Typhus and Brucellosis.—Knight and associates report that in the summer of 1948 in the course of an investigation of the antimicrobial therapy of typhoid fever with various drugs, 11 patients with typhus and 5 with brucellosis were treated with aureomycin. The studies were conducted in Mexico. The administration of aureomycin to 11 patients with typhus (presumably murine) was followed in every instance by prompt defervescence and complete recovery. No instances of relapse were observed, although in 7 cases the total period of antimicrobial therapy was limited to forty-eight hours or less. In 4 patients with acute brucellosis, 1 of whom had meningo-

encephalitis, a similar prompt disappearance of the manifestations of the infection occurred soon after the start of aureomycin therapy. Since this material was submitted for publication, 8 additional patients with typhus have been successfully treated with aureomycin. Seven of these patients were treated with oral doses ranging from 100 to 160 mg. per kilogram of body weight per day, for intervals of thirty-six to forty-eight hours. These patients all showed rapid improvement after therapy. One patient in the eighth day of her illness received aureomycin intravenously. She was given doses of 200 mg. at eight hour intervals during the first day and at twelve hour intervals during the second day. Improvement was rapid; by the time the last dose was administered she was asymptomatic and permanently afebrile. Other patients were treated with lower oral dosages. It appears that the lowest fully effective dose may lie somewhere between 50 and 100 mg. per kilogram per day for a short interval of therapy.

Acetylsalicylic Acid in Rheumatic Fever.—Hoffman and associates present observations on 80 adult patients with acute rheumatic fever who were treated with acetylsalicylic acid until disappearance of clinical symptoms. Of 65 patients started with control tablets of acetylsalicylic acid, 8 complained of gastric distress following ingestion of the drug. This distress disappeared when tablets which contained acetylsalicylic acid and aluminum hydroxide were taken. For most of the period of therapy in all patients, acetylsalicylic acid plus aluminum hydroxide was administered. Some symptoms of salicylism occurred in almost all patients when the plasma salicylate level was more than 30 mg. per hundred cubic centimeters. Only 41 patients could be maintained at this level; 39 had to be given doses that produced levels under 25 mg. per hundred cubic centimeters. The sedimentation rate subsided to normal in a slightly larger proportion of patients in the group with high plasma salicylate levels. The prothrombin concentration was only slightly affected by acetylsalicylic acid therapy. A moderate fall in the serum bicarbonate level occurred in most cases, associated with an elevated serum chloride and a slightly diminished serum sodium. The blood p_H was usually normal. The urine was usually acid. It is believed that salicylate produces a primary hyperpnea with alkalosis but that the accumulated salicylate produces a fixed acid acidosis and that the two effects are mutually compensatory. The apparent salicylate clearance after acetylsalicylic acid therapy is only about 3 per cent of the creatinine clearance when the urine is highly acid. It increases three to eight times when the urine is alkalinized with sodium bicarbonate. Most of this increase is in free salicylate. Alkalinization is therefore of prime importance in the treatment of salicylate poisoning.

Am. J. Roentgenol. & Rad. Therapy, Springfield, Ill.

61:443-590 (April) 1949

Hemosiderosis of Lung Due to Mitral Disease: Report of 6 Cases Simulating Pneumoconiosis. E. P. Pendergrass, E. L. Lame and H. W. Ostrum.—p. 443.
Apical Form of Bronchopulmonary Cancer. N. Romano and R. Eyherabide.—p. 457.
Case of Carcinosarcoma of Esophagus. A. P. Stout, G. H. Humphreys II and L. A. Rottenberg.—p. 461.
*Mass Roentgenologic Survey of Gastrointestinal Tract to Detect Cancer of Stomach. S. Moore.—p. 470.
Paraplegic Neuroarthropathy. J. Solovay and H. U. Solovay.—p. 475.
Double Contour, Cupping and Spurring in Roentgenogram of Long Bones in Infants. K. Glaser.—p. 482.
Sesamoid Bones of Hands and Feet. C. A. Hubay.—p. 493.
Occupational Calcareous Peritendinitis of Feet: Case Report. C. F. Miller.—p. 506.
Kaposi's Sarcoma: Report of 2 Cases. W. H. Boone and E. A. Kratzman.—p. 511.
Radium Therapy for Carcinoma of Bartholin's Glands. H. H. Bowing, R. E. Fricke and T. J. Kennedy.—p. 517.
Effects of Repeated Low Doses of Neutrons on Estrous Cycle of White Rat. J. L. Leitch, D. M. Gay and G. A. Neville.—p. 530.
Pharmacologic Reactions of Serums and Drugs Irradiated with Roentgen Rays of Varying Wavelength. D. I. Macht and M. Ostro.—p. 534.
Thimble Chamber Calibration on Soft Roentgen Rays. F. H. Day.—p. 543.
Negative Feedback Dosage Rate Meter Using Small Ionization Chamber. H. E. Johns, E. K. Darby and J. J. S. Hamilton.—p. 550.

Roentgenologic Survey in Detection of Gastrointestinal Cancer.—Moore reviews 30,985 examinations of the gastrointestinal tract performed from 1916 to 1947, inclusive. Roentgen diagnosis of carcinoma of the gastrointestinal tract was made in 1,352 of a total of 14,337 pathologic cases. Reviewing this material made it evident that the stomach will not lend itself to mass roentgenologic surveys for many reasons. The time and labor required would be great. The fact that there is a high incidence of cancer in the other segments of the gastrointestinal tract is often ignored, yet if all gastric cancers were diagnosed early by mass methods there would remain a large number of cancers elsewhere in the tract that would escape detection. The material reviewed consisted largely of patients with some symptoms ascribable to the alimentary tract; yet, the percentage of cancer was low. The author concludes that gastrointestinal examination is unsuitable for mechanization such as would be the case with mass survey technics. Gastric cancer of the one type which seems to be suitable for detection by mass survey methods comprises but a small part of the problem.

American Journal of Surgery, New York

77:543-678 (May) 1949

Vagina in Reconstructive Surgery: Histologic Study of Its Structural Components. J. V. Ricci, J. R. Lisa, C. H. Thom Jr. and W. Kron.—p. 547.
Cesarean Sections—1937 to 1946. I. Daichman and W. Pomerance.—p. 555.
Pneumatosis Intestinalis: Roentgen Diagnosis and Surgical Management. A. I. Gazin, W. S. Brooke, H. H. Lerner and P. B. Price.—p. 563.
Malignant Tumors of Small Intestine. I. E. Siris.—p. 573.
Does Bowel Prevent Outward Diffusion of Gas from Within Balloon of Intestinal Tubes? Experimental Study. M. O. Cantor, E. R. Phelps and R. H. Esling.—p. 585.
Further Study of Suspensory Muscle of Duodenum. J. C. Haley and J. H. Perry.—p. 590.
Cholecystostomy: Study of Patients Ten to Sixteen Years Later. J. G. Donald and W. T. Fitts Jr.—p. 596.
Further Studies in Articular Replacement. S. S. Hudack and J. W. Blunt Jr.—p. 600.
Surgical Analysis of 124 Cases of Proven Acute Cholecystitis. V. D'Ingianni, I. L. Fontenelle and H. A. D'Ingianni.—p. 608.
Pheochromocytoma. R. F. Hedin and R. V. Sherman.—p. 614.
Review of Meckel's Diverticulum: Report of 4 Cases. W. Fry.—p. 620.
Surgical Aspects of Peripheral Vascular Disease. G. H. Martin.—p. 624.
Glycerite of Hydrogen Peroxide: Comparison of Its Bacteriotoxic Effect on Clostridia with That of Other Antiseptics. E. A. Brown, R. E. Skiffington and W. B. Krabek.—p. 630.
Surgical Management of Moribund Burn Patient. L. W. Eisenstodt.—p. 634.
Biliary Surgery Through Transverse Incision. V. J. Hittner.—p. 640.

American Review of Tuberculosis, New York

59:353-468 (April) 1949

Diagnosis and Treatment of Lung Tumor. R. Adams.—p. 353.
*Observations on Causes of Dyspnea in Chronic Pulmonary Granulomatosis in Beryllium Workers. R. A. Bruce, F. W. Lovejoy Jr., G. B. Brothers and T. Velasquez.—p. 364.
Role of Pulmonary Cavitation in Development of Bacterial Resistance to Streptomycin. W. L. Howard, F. Maresh, E. E. Mueller and others.—p. 391.
*Sensitivity of Tubercle Bacilli to Streptomycin: Influence of Various Factors Upon Emergence of Resistant Strains. K. S. Howlett Jr., J. B. O'Connor, J. F. Sadusk Jr. and others.—p. 402.
Coexisting Disseminated Coccidioidomycosis and Tuberculosis: Report of Case. G. M. Firestone and E. S. Benson.—p. 415.
Viability of Tubercle Bacilli in Embalmed Human Lung Tissue. G. M. Meade and W. Steenken Jr.—p. 429.
Acquired Resistance of M. Tuberculosis to Streptomycin in Vitro and Its Behavior in Experimental Infections. E. W. Emmart, W. T. McClosky, M. I. Smith and J. E. Lieberman.—p. 438.
Routine Examination of Sputum for Acid-Fast Bacilli. D. G. Freiman and M. Pinner.—p. 449.
Study of Bacteriostatic and Bactericidal Activity of Promin, Diasone, Sulfathiazole, Sulfaguanidine and Streptomycin on H-37V Strain of M. Tuberculosis. K. T. Sasano.—p. 461.

Dyspnea in Pulmonary Granulomatosis in Beryllium Workers.—Bruce and associates report observations on the cardiorespiratory function of 6 patients with chronic delayed pulmonary granulomatosis due to beryllium. Four of these patients had contact with beryllium compounds under industrial working conditions. The other 2 were "neighborhood cases"; the patients had had contact with beryllium compounds only from atmospheric contamination in close proximity to a manufacturing plant. The duration of respiratory distress in these 6 patients ranged between one and six years. The etiology was presumed in most cases by exclusion of all differential diagnoses and was established in 1 patient by identification of trace amounts of beryllium in the urine, and in another patient beryllium was recovered from kidney stones. These patients were hospitalized for two weeks to three months. Breathing

capacity was measured; bronchospirometry was performed; measurements of alveolar pressure-velocity relationships were obtained; blood oxygen and carbon dioxide contents and capacities were measured. Cardiac studies included serial electrocardiograms with complete chest leads, ballistocardiograms, pneumocardiograms and intracardiac pressure-pulse recordings. Venous pressure and circulation times were also measured. The results of these studies are essentially in accord with those observed by other investigators of a similar group of patients. The main deviation from normal is the hyperventilation. Diminished arterial oxygen saturation is a function of abnormally increased alveolar-arterial gradient for oxygen and contracted lung volume, particularly complementary air. One of these patients exhibited polycythemia as a compensatory mechanism. Various stages of cor pulmonale, including congestive heart failure due to increased pulmonary resistance, were observed. An unusual response to intravenous digoxin and the lack of benefit from cytochrome C therapy are recorded. The authors call attention to variations in response to exercise and similarities to functional impairment of other chronic pulmonary disease.

Streptomycin-Resistant Tubercle Bacilli.—Howlett and associates call attention to the frequent emergence of streptomycin-resistant strains of tubercle bacilli in tuberculous patients treated with streptomycin. Interest thus far has been largely concentrated on variations in the daily dose, the frequency of administration and the total duration of streptomycin treatment. Little attention has been given to possible influences inherent in the patient or in the tuberculous disease. The chief purpose of the investigation reported here was to survey two relationships: (1) between the incidence of streptomycin-resistant tubercle bacilli and the treatment regimen employed and (2) between the incidence of streptomycin-resistant tubercle bacilli and the type of pulmonary tuberculosis being treated. In a group of 28 patients treated on a regimen of 1.8 or 2.0 Gm. of streptomycin daily for one hundred and twenty days, resistant strains of tubercle bacilli eventually occurred in 8. In a group of 47 patients treated on a regimen of 1.0 Gm. of streptomycin daily for forty-two days (later revised to 20 mg. per kg. of body weight daily for forty-five days), resistant strains eventually occurred in 13. A reduction in the duration of streptomycin treatment from one hundred and twenty days to forty-two (or forty-five) days has been considerably less successful than had been hoped in reducing the incidence of resistant tubercle bacilli. A correlation has been observed between the incidence of resistant tubercle bacilli and the type of tuberculosis treated. Resistant strains have emerged in a high proportion of patients who had caseation or cavity in pretreatment roentgenograms. In a group of 56 such patients, treated on the several regimens employed in this study, strains uninhibited by 10 micrograms of streptomycin per cubic centimeter of culture medium eventually occurred in 33. In contrast, and regardless of the treatment regimen employed, strains uninhibited by 10 micrograms per cubic centimeter or less have occurred thus far in none of 31 patients who had no frankly caseous or cavernous lesions prior to treatment.

Archives of Ophthalmology, Chicago

41:253-392 (March) 1949

Pharmacology and Toxicology of Cornea: Contemporary Concepts. K. C. Swan.—p. 253.
*Inheritance of Arachnodactyly, Ectopia Lentis and Other Congenital Anomalies (Marfan's Syndrome) in E. Family. F. C. Lutman and J. V. Neel.—p. 276.
Morphologic Changes in Cells of Corneal Epithelium in Wound Healing. W. Buschke.—p. 306.
Myxosarcoma of Eyelid. W. Moehle.—p. 317.
Motais-Parinaud Type of Operation for Ptosis: Report on 35 Cases. R. N. Berke.—p. 324.
Progressive Muscular Dystrophy Involving Extraocular Muscles: Report of Case. S. Gartner and E. Billet.—p. 334.
Traumatic Choroiditis: Review of Literature and Report of 10 Cases. P. Tower.—p. 341.

Congenital Anomalies.—Lutman and Neel present the pedigree of a family of 40 persons, 17 of whom probably had Marfan's syndrome which is characterized by arachnodactyly, ectopia lentis, cardiac abnormalities and other congenital defects. There was a great variability in the expression of the syndrome in the affected members; of the 16 persons, exclusive of the male progenitor of the line, 5 exhibited the triad of arachnodactyly, dislocated lenses and cardiac abnormalities; 9 exhibited only two aspects of the triad, while in the remaining 2 the diagnosis rested on the observation of a single component of the triad. Some of the members were so mildly affected that the diagnosis would be unsuspected or in doubt were it not for their genetic background. Ocular anomalies observed in all persons studied, in addition to either ectopia lentis or coloboma of the lens, were abnormal zonular fibers, an iris lacking in the usual surface trabecula and crypts, deficiencies of uveal pigment, particularly at the periphery of the iris, and amblyopia. In several cases these were accompanied with other ocular defects. The syndrome is inherited as though due to one or more dominant autosomal genes. Although a final decision is not possible, the bulk of the evidence suggests that the entire syndrome may be due to one gene only, the expression of which is greatly influenced by other genetic and possibly environmental factors. This syndrome would quickly disappear through natural selection unless there was a relatively high mutation rate from normal to the gene responsible for the syndrome. The many isolated cases which have been reported are thought for the most part to represent results of this mutation process.

Archives of Otolaryngology, Chicago

49:335-446 (April) 1949

Hydrodynamics and Hearing: I. Operative Relief of Otosclerotic and Nonotosclerotic Deafness and Its Relationship to Hydrodynamic Hypothesis of Hearing; Suggested Explanation for (*a*) Intimate Association of Organs of Balance and Organ of Hearing and for (*b*) Function of Incus. O. Popper.—p. 335.
Transtympanic Approach and Fenestration: II. Current Technic. O. Popper.—p. 350.
Acoustic, Vestibular and Other Problems Concerning Otosclerosis and Its Surgical Treatment According to Popper's Method: I. Popper's Operation for Otosclerosis. R. Lund.—p. 380.
Id.: II. Acoustic Function Before and After Operation for Otosclerosis. H. Ewertsen.—p. 393.
Id.: III. Vestibular Function Prior to and Following Operation for Otosclerosis. H. Rasmussen.—p. 402.
Id.: IV. Biochemical Conditions in Patients with Otosclerosis. N. Riskaer.—p. 414.
Id.: V. Conditions of External Auditory Meatus and Tympanic Membrane in Patients with Otosclerosis. S. Selsø.—p. 420.
Actinomycosis Involving Ethmoid and Maxillary Sinuses: Report of Case. R. B. Lewy and E. L. Manning.—p. 423.
Interpretation of Hearing Tests. S. R. Guild.—p. 431.

Archives of Pathology, Chicago

47:205-306 (March) 1949

Formation of Hemosiderin and Hematoidin After Traumatic and Spontaneous Cerebral Hemorrhages. G. Strassmann.—p. 205.
Significance of Ehrlich's Reaction in Cases of Melanuria. A. J. Lea.—p. 211.
Nonparasitic, Noncancerous Cystic Tumors of Spleen. W. L. Bostick and S. P. Lucia.—p. 215.
Nuclear Size in Tetanized and in Curarized Skeletal Muscle. R. Altschul.—p. 223.
Organoid Differentiation of Fetal Lung: Histologic Study of Differentiation of Mammalian Fetal Lung in Utero and in Transplants. W. R. Waddell.—p. 227.
*Lesions Induced in Rabbits by Cholesterol Feeding, with Special Reference to Their Origin. A. Kuntz and N. M. Sulkin.—p. 248.
The Phenomenon of Leukergy. L. Fleck and Z. Murczynska.—p. 261.
Changes in Capsule of Lymph Node in Experimental Hyperplasia. W. J. Furuta.—p. 273.
Distribution of Lymphatics of Human Kidney as Shown in Case of Carcinomatous Permeation. A. J. Rawson.—p. 283.

Lesions Induced in Rabbits by Cholesterol Feeding.—Kuntz and Sulkin found that in rabbits fed cholesterol daily in addition to a rabbit chow hypercholesteremia and hypertension developed. In those fed 1 Gm. of cholesterol daily, atherosclerotic lesions appeared in the aorta and other large arteries within thirty days. As the process advanced, lesions appeared also in small arteries. The initial atheroma consisted mainly of a few foam cells in the intima. As the number of foam cells increased, a thick intimal plaque was formed. Collagenous fibers soon appeared in the plaque. Associated with these fibers were some fibroblasts. The late lesion included a large percentage of fibrous tissue, including numerous fibroblasts. In sections the late intimal plaque exhibited stratification due to alternate arrangement of the fibrous tissue and the foam cells. Early atherosclerotic lesions were limited to the intima;

many of the older lesions extended into the media. The data support the assumption that the foam cells observed in atherosclerotic lesions are derived locally from the endothelium. The fibrous tissue is derived from connective tissue elements of the intima and the media. Xanthomatosis occurred in all rabbits with advanced atherosclerosis. The data relative to the origin of the xanthoma cells support the assumption that these also arise locally from the mesenchymal epithelium and from undifferentiated cells of the synovial membranes. In rabbits with advanced atherosclerosis, lesions characterized by foam cells developed also in viscera, particularly in the liver, spleen, adrenal glands and kidneys. There also the foam cells appeared to arise locally. The autonomic ganglions and nerves exhibited a succession of alterations which in the later phases of cholesterol feeding suggested functional depression of the cells.

Connecticut State Medical Journal, Hartford

13:409-512 (May) 1949

Management of Acute Injuries of Hand. M. L. Mason.—p. 414.
Some Reactions to Anti-Biotics. L. Goldman.—p. 420.
Bronchopulmonary Segments and Their Relation to Disease. R. H. Jordan.—p. 424.
Dynamic Therapeutics in Chronic Disease Pay Dividends. H. A. Rusk.—p. 431.
Brucellosis Treated by Aureomycin: Case Report. H. Boyd and J. Prignano.—p. 435.
Cancer in Lactating Breast. P. G. McLellan.—p. 437.
Signs and Portents in Medicine. J. E. Bryan.—p. 441.

Journal of Bone and Joint Surgery, Boston

31-A:225-458 (April) 1949. **Partial Index**

Tendon Transfers and Arthrodeses in Combined Median and Ulnar Nerve Paralysis. J. W. Littler.—p. 225.
Surgical Approaches to Shoulder Joint. L. C. Abbott, J. B. deC. M. Saunders, H. Hagey and E. W. Jones Jr.—p. 235.
Tuberculosis of Spine: Analysis of Cases Treated Surgically. D. M. Bosworth and J. Levine.—p. 267.
Spondylitis, Pathologic Ossification, and Calcification Associated with Spinal-Cord Injury. D. J. Abramson and S. Kamberg.—p. 275.
Myositis Ossificans in Paraplegics. L. F. Miller and C. J. O'Neill.—p. 283.
Spontaneous Sacro-Iliac Obliteration in Patients with Tuberculosis. A. S. Isaacson and W. M. Whitehouse.—p. 306.
Blade-Plate Fixation in Non-Union and in Complicated Fractures of Supracondylar Region of Femur. A. R. Altenberg and R. L. Shorkey.—p. 312.
Etiology of Congenital Dislocation of Hip. C. E. Badgley.—p. 341.
Congenital Dysplasia of Hip Joint: Relationship Between Congenital Subluxation and Congenital Dislocation. V. L. Hart.—p. 357.
Injuries of Lateral Ligaments of Ankle: Clinical and Experimental Study. M. H. Leonard.—p. 373.
Some Obstetrical Injuries to Long Bones. S. T. Snedecor and H. B. Wilson.—p. 378.
Mortised Transfacet Bone Block for Lumbosacral Fusion. E. B. McBride.—p. 385.
Aspects of Physical Reconditioning. M. J. Stewart.—p. 394.
Pseudarthrosis Following Spine Fusion. W. A. L. Thompson and E. L. Ralston.—p. 400.
Muscle Transplantation for Triceps Palsy: Technic of Utilizing Latissimus Dorsi. P. H. Harmon.—p. 409.
*Calcification of Bursae of Knee. T. Norley and W. H. Bickel.—p. 417.
Amputation for Discrepancy of Limb Length in Tuberculosis of Hip. F. A. Chandler and T. A. Fox.—p. 420.
Successful Prosthesis for Sacro-Iliac Disarticulation (Hemipelvectomy). R. A. Wise.—p. 426.
Treatment of Congenital Club-Foot: Nine Years' Experience with Modification of Denis Browne Method and Splint. S. A. Thomson.—p. 431.

Calcification of Bursae of Knee.—According to Norley and Bickel a search of the literature failed to disclose any report of calcification of the bursae of the knees. Brantigan and Voshell stated that calcification of the superior bursa beneath the tibial collateral ligament might "account for certain cases of Pellegrini-Stieda disease." Search of the records of the Mayo Clinic yielded 8 cases of calcification of the bursae of the knee. The patients complained of progressive pain on motion, of swelling and of limited motion. Physical examination usually revealed a tender swelling over the involved bursa. Calcification within the bursa was not usually suspected until its presence was revealed in the roentgenogram. One patient had recurrent painless swelling without any localizing signs, and the roentgenograms revealed calcification of the bursa over the medial condyle of the femur. Four patients gave a history of injury and most commonly of repeated trauma over a period of years. Locations of the calcified bursae were: prepatellar bursae in 2 cases, infrapatellar bursa in 1, bursae over the medial femoral condyle in 4 and bursa over the lateral epicondyle in 1. Needling and injection of procaine hydrochloride or surgical excision may be curative; the more conservative means should be used first if the symptoms are not too severe.

Journal of Clin. Endocrinology, Springfield, Ill.

9:301-402 (April) 1949. **Partial Index**

Estrogen-Producing Sertoli Cell Tumors (Androblastoma Tubulare Lipoides) of Human Testis and Ovary. Homologous Ovarian and Testicular Tumors. III. G. Teilum.—p. 301.
Cortical Steroid Excretion in Edema of Pregnancy, Pre-Eclampsia and Essential Hypertension. L. Tobian Jr.—p. 319.
*Therapeutic Studies in Hyperthyroidism: Propylthiouracil. P. Starr, D. W. Petit, L. Meister and R. L. Stirrett.—p. 330.
Use of Tracer Doses of Radioactive Iodine, I^{131}, in Study of Normal and Disordered Thyroid Function in Man. S. C. Werner, E. H. Quimby and C. Schmidt.—p. 342.
Antihormone Formation Complicating Pituitary Gonadotropin Therapy in Infertile Men. II. Effect on Number of Sperm, Morphology of Testis and Urinary Gonadotropins. E. C. Jungck, W. O. Maddock, C. G. Heller and W. O. Nelson.—p. 355.
Relative Independence of Sodium and Chloride Excretion. J. W. Goldzieher and G. C. H. Stone.—p. 368.

Propylthiouracil in Hyperthyroidism.—Starr and co-workers treated 40 patients having varieties of hyperthyroidism with propylthiouracil. The average duration of treatment of the entire series was six and one-half months, ranging from one to fifteen months. The dosage of the drug ranged from 150 to 600 mg. daily. Hyperthyroidism was controlled in 21 of 28 patients for from one to ten months during the administration of the drug. The disease was not completely controlled, as indicated by abnormal protein-bound iodine levels in the serum in 7 of 28 patients. Granulocytopenia, evidenced by polymorphonuclear cells ranging from 14 to 48 per cent, was found in 6 of the 40 patients to whom the drug was given, indicating a toxic effect on the bone marrow in 15 per cent. Medication was not interrupted in any patient because of the granulocytopenia. The initial fall of protein-bound blood iodine during the first twenty-four days of treatment was not significantly greater during therapy with 600 mg. of propylthiouracil a day than with 150 mg. a day. A relapse, judged by both clinical and chemical observations, occurred in nearly every case in which administration of the drug was discontinued, even when control had been complete chemically for as long as ten months. General use of the drug in preparation for secondary thyroidectomy is justified. Its use as a prolonged treatment in the hope that hyperthyroidism will be cured or that an indefinite remission will be induced seems unjustified.

Journal of Experimental Medicine, New York

89:369-460 (April) 1949. **Partial Index**

Immobilization of Treponema Pallidum in Vitro by Antibody Produced in Syphilitic Infection. R. A. Nelson Jr. and M. M. Mayer.—p. 369.
Studies on Acute Disseminated Encephalomyelitis Produced Experimentally in Rhesus Monkeys. IV. Disseminated Encephalomyelitis Produced in Monkeys with Their Own Brain Tissue. E. A. Kabat, A. Wolf and A. E. Bezer.—p. 395.
Additive Effects of Certain Transforming Agents from Some Variants of Pneumococcus. H. E. Taylor.—p. 399.
Electron Microscope Study of Salivary Gland Chromosomes by Replica Method. S. L. Palay and A. Claude.—p. 431.
Type-Specific Protein from Pneumococcus. R. Austrian and C. M. MacLeod.—p. 439.

89:461-560 (May) 1949

Studies on Mechanism of Shwartzman Phenomenon. L. Thomas and C. A. Stetson.—p. 461.
Effect of Lithium Periodate on Crystalline Bovine Serum Albumin. W. F. Goebel and G. E. Perlmann.—p. 479.
Mechanism of Active Cerebral Immunity to Equine Encephalomyelitis Virus. I. Influence of Rate of Viral Multiplication. R. W. Schlesinger.—p. 491.
Id. II. Local Antigenic Booster Effect of Challenge Inoculum. R. W. Schlesinger.—p. 507.
Nutrition of Host and Natural Resistance to Infection. IV. Capability of Double Strain Inoculation Test to Reveal Genetically Determined Differences in Natural Resistance to Infection. H. A. Schneider.—p. 529.
Diffuse Glomerulonephritis Produced in Rabbits by Massive Injections of Bovine Serum Gamma Globulin. R. H. More and D. Waugh.—p. 541.
Cardiac Lesions Produced in Rabbits by Massive Injections of Bovine Serum Gamma Globulin. R. H. More, D. Waugh and S. D. Kobernick.—p. 555.

Journal of Nervous and Mental Disease, New York

109:291-382 (April) 1949

Early Reversible Paranoiac Reactions: Detailed Study of Six Case Histories and Eight Cases. H. Rosen and H. E. Kiene.—p. 291.
Effect of Alpha: Beta-Dihydroxy-Gamma-(2-Methylphenoxy) Propane (Lissephen) on Excitation of Motor Cortex and Conduction Through the Pyramids. I. Finkelman and N. B. Dobin.—p. 323.
Action of Alpha: Beta-Dihydroxy-Gamma-(2-Methylphenoxy)-Propane (Lissephen) on Peripheral Nerves. I. Finkelman and A. J. Arieff. —p. 326.
Psychobiologic Dysfunction in Children. J. R. Jacobson and H. G. Pratt. —p. 330.
*Sedative Insulin Treatment of Anxiety in Anxiety Neurosis. G. J. Martin.—p. 347.

Sedative Insulin in Anxiety Neurosis.—Martin treated 210 patients with anxiety neurosis with insulin. A control group of 170 similar cases was studied. Only the more easily observed symptoms of anxiety such as tremulousness, restlessness, apprehension, hyperhidrosis, insomnia and anorexia were considered within the scope of the author's study. The 210 experimental patients received 5,918 treatments of insulin at an average dosage level of 55 units. Most patients received between 30 and 40 treatments. The patient was given an initial dose of 10 units of insulin and this was increased 10 units daily until a maximum tolerated dose of between 55 and 70 units was reached. The patient was then maintained on this dose until no further improvement was noted. Both the experimental and the control group participated in the general psychotherapeutic program designed for open ward psychiatric patients. The experimental group showed the greatest amount of improvement in all studies. The less predisposed patients with an illness of five to ten months' duration, starting in combat or being aggravated by combat, responded best. Sedative insulin is considered only a small item in the general treatment program, but when used within the program it has definite therapeutic value. Sedative insulin afforded a standard, simple, easily managed adjunct to therapy. It is suggested that a satisfactory sedative insulin program could be devised for use on an outpatient basis or in the general civilian hospital.

Journal of Pediatrics, St. Louis

34:393-528 (April) 1949

Effect of Milk Supplements on Growth of Children with Nutritive Failure: The Wetzel Grid Findings. T. D. Spies and S. Dreizen. —p. 393.
Antihistaminic Drugs in Pediatric Allergy. L. H. Criep and T. Aaron. —p. 414.
*Leukemia in Childhood: Clinical and Roentgenographic Study of Seventy-Two Cases. J. H. Dale Jr.—p. 421.
Intravenous Procaine in Children. D. Schrum.—p. 433.
Methyl Testosterone in Treatment of Premature Infants. J. Hardy and L. Wilkins.—p. 439.
Carbohydrate Supplements (Lactose and Starch Hydrolysates) in Infant Feeding: Blood Sugar Changes Following Administration of Carbohydrate Supplements in Various Milk Media. S. Natelson, M. Sherman and B. Kramer.—p. 443.
Fungus Studies in Atopic Dermatitis: Failure to Demonstrate Pathogenic Fungi in the Lesions. H. H. Perlman.—p. 458.
*Fluorescein Circulation Time in Normal and Pathologic Conditions in Infants and Children, Including Various Types of Congenital Malformations of the Heart. B. M. Gasul, J. J. Marino and J. R. Christian.—p. 460.
Amelia: Review of Literature and Report of Case. H. H. Pomerance and H. Soifer.—p. 465.
Solitary Renal Ectopia and Nephrotic Syndrome. R. H. Kunstadter and I. J. Shapiro.—p. 470.

Leukemia in Childhood.—Dale reports 72 infants and children, 38 boys and 34 girls, with leukemia who were observed from 1932 to 1948. The age incidence ranged from 10 months to 12¼ years. The peak was in the third year of life, and the majority of cases occurred in the first five years. Thirty-five patients died within one year and 27 within six months of the onset of symptoms. Only 3 patients survived one and one-half years or longer. The course of leukemia in childhood is characteristically acute, rapidly progressive and fatal within a short period from the onset. Childhood leukemia has no characteristic symptom complex and is often protean in its early manifestations, closely simulating many of the acute and subacute diseases of this period. The presence of fever, bone and joint swelling and tenderness, and a systolic heart murmur in the absence of lymphadenopathy, hepatomegaly and splenomegaly in some patients suggested the diagnosis of acute rheumatic fever. Sixty-nine of the patients had varying degrees of anemia at admission, and the remainder had anemia during the course of the disease. Sternal marrow aspiration biopsies were employed in 54 patients, and in all abnormal leukocytes were demonstrated. The marrow was hyperplastic in the majority of cases with a depression of erythropoietic tissue paralleling the peripheral anemia. Osseous changes in childhood leukemia, although frequent, are not specific. A transverse band of diminished density in the metaphyses of the long bones was the most frequently observed lesion. Osteolysis was next in order, and periosteal elevation with new bone formation was the third most frequent roentgenographic change. Roentgenologic examination of the skeletal system, although not as specific or reliable as sternal marrow aspiration, aids materially in the detection of osseous changes suggestive of abnormal marrow activity and points to the necessity for a thorough hematologic study of the patient. Roentgen examination of the knee area provides a helpful screening technic in the investigation of all suspected cases of leukemia.

Fluorescein Circulation Time.—Gasul and co-workers measured the fluorescein circulation time, i. e., the time between the injection of sodium fluorescein into the antecubital vein and the first appearance of the dye on the patient's lips, in 107 patients between 15 days and 13 years of age, 57 of whom had demonstrable cardiac disease, 50 of whom had no demonstrable cardiac disease. The calculated dose of the test substance was approximately 0.7 cc. per 10 pounds (5 Kg.) of body weight. In the normal noncardiac group, the average circulation time from the neonatal period through 2 years of age was 6.5 seconds. From 3 to 13 years, the average was 8.5 seconds. In tetralogy of Fallot where the aorta is dextraposed, or in complete transposition of the great vessels where the aorta comes off the right ventricle, as well as in triscupid atresia with an interauricular defect, the fluorescein circulation time is shortened to an average of 3.7 seconds. The fluorescein circulation time is appreciably altered in interauricular or interventricular septal defects or in patent ductus Botalli, coarctation of the aorta or Lutembacher's syndrome. The circulation time is not appreciably altered in acute or convalescent rheumatic heart disease except in congestive heart failure, where it is definitely prolonged, with an average of 17.7 seconds as compared with an average of 9.2 seconds in the compensated cases. The fluorescein circulation time in infancy and childhood is a simple, nontoxic, inexpensive, objective procedure.

Military Surgeon, Washington, D. C.

104:331-414 (May) 1949. **Partial Index**

Experience with Vagotomy in Treatment of Peptic Ulcer. P. A. Bergman, S. W. French III and S. F. Seeley.—p. 331.
Aircrew Maintenance—Problem of Aviation Preventive Medicine. W. J. Kennard.—p. 336.
Fundamental Questions in Intestinal Obstruction. W. F. Bowers. —p. 341.
Newer Concepts with Reference to Movement of Sick and Wounded by Air. K. E. Pletcher.—p. 344.
Ocular Manifestations of Intracranial Injury. J. G. Bryson.—p. 348.
Promotion of Healing Following Intestinal Surgery. E. J. Poth.—p. 358.
Benzedrine Habituation. C. T. Brown.—p. 365.
Intestinal Parasites in Prison Population. R. L. Lawrence and J. H. Hudgens.—p. 371.
Effect of Malnutrition on Calcification and Growth of Teeth During Childhood. H. C. Largeman.—p. 373.

Nebraska State Medical Journal, Lincoln

34:117-156 (April) 1949

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34:157-200 (May) 1949

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Portal Hypertension. H. H. Davis.—p. 170.

SYMPOSIUM ON MULTIPLE INJURIES IN AUTOMOBILE ACCIDENTS

Brain Injuries. J. J. Keegan.—p. 175.
Injuries to Spine and Pelvis: W. L. Sucha.—p. 177.
Chest Injuries. J. D. Bisgard.—p. 180.
Injuries of Abdominal Viscera. F. C. Hill.—p. 184.
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New England Journal of Medicine, Boston

240:589-628 (April 14) 1949

Occurrence of Infection After Pulmonary Resection: Study of Effectiveness of Sulfonamides and Antibiotic Agents During Six-Year Period (1942-1947). C. C. Miller and R. H. Sweet.—p. 589.
Acquired Afibrinogenemia in Pregnancy. W. C. Moloney, W. J. Egan and A. J. Gorman.—p. 596.
Nitrate Methemoglobinemia. H. Marcus and J. R. Joffe.—p. 599.
Streptomycin in Treatment of Salmonella Enteritis in Infants. S. Ross, F. G. Burke, E. C. Rice and others.—p. 602.
Surgery in Chronic Arthritis. J. G. Kuhns.—p. 605.
(Squamous-Cell Carcinoma of Lung). Operation: Lobectomy. Acute Coronary Thrombosis.—p. 611.
Malignant Lymphoma, Reticulum-Cell-Sarcoma Type, of Testis, Stomach and Retroperitoneal Lymph Nodes.—p. 614.

240:629-668 (April 21) 1949

*Cardiac Aneurysm. M. Caplan and P. M. Sherwood.—p. 629.
Osteitis Pubis. M. Abrams, I. Sedlezky and D. B. Stearns.—p. 637.
Werner's Syndrome: Report of 2 Cases. J. Schott and S. Dann.—p. 641.
Peripheral Vascular Disease. R. R. Linton.—p. 645.
Chronic Thyroiditis, Hashimoto Type. Hyperplasia of Thyroid Gland. —p. 655.
Lower-Nephron Nephrosis.—p. 658.

Cardiac Aneurysm.—Caplan and Sherwood cite *2* patients in whom ventricular aneurysm was diagnosed during life. Formerly it was rarely recognized during life, but now it is frequently suspected before death and it no longer has the dire prognosis commonly associated with the condition in the past. Practically all the symptoms in patients with cardiac aneurysms can be attributed to the underlying cardiac lesion. The aneurysm per se is asymptomatic except for occasional development of pain in the region of the apex. The anginal syndrome of left ventricular failure is not produced by the aneurysm but is related to the coronary artery or myocardial disease. The authors discuss the increased incidence, physical and roentgen observations and clinical course of cardiac aneurysm. Certain criteria for the antemortem diagnosis, as well as the brighter outlook regarding prognosis and longevity, are stressed. Patients are not incapacitated by their cardiac aneurysms. In view of the recent emphasis on early ambulation after myocardial infarction, many patients in whom ventricular aneurysms have developed have received inadequate bed rest after the acute episode of infarction. During the period of myomalacia every precaution must be taken to support the weakened myocardium, and undoubtedly bed rest reduces the work of the heart and allows a firmer scar to develop. It will be interesting to note the effect on the incidence of rupture of ventricular aneurysm of the introduction of anticoagulant therapy for myocardial infarction. Reduction of clot formation within the aneurysm theoretically may result in a thin-walled sac that does not have the support of a firm, lamellated clot. This type, having only the pericardium as its support, tends to increase its size and is more likely to rupture. Late embolic manifestations may be prevented by anticoagulant therapy.

New Jersey Medical Society Journal, Trenton

46:223-268 (May) 1949

Diagnostic Difficulties of Non-Paralytic Poliomyelitis. H. Simon, E. L. Smith and H. O. Bell.—p. 225.
Hemochromatosis: Case Report. H. S. Read, L. M. Walker and C. B. Whims.—p. 230.
Carcinoma of Cervix. L. J. Levinson, W. M. Brams and B. Levinstone. —p. 234.
Differential Diagnosis of Peripheral Vascular Diseases. W. Redisch. —p. 238.
Importance of Sigmoidoscopy. R. A. Hopping.—p. 244.
Laboratory Diagnostic Aids for General Practitioner. T. K. Rathmell and J. P. Greeley.—p. 245.
Religion and Medicine. H. A. Murray.—p. 248.

Occupational Therapy & Rehabilitation, Baltimore

28:109-226 (April) 1949. **Partial Index**

Occupational Therapy for Lobotomy Patients. R. W. Hyde and A. C. Wood.—p. 109.
*Rehabilitation on the Job. G. F. Keatinge.—p. 125.
Eating Devices for Paraplegic Patient. H. R. Shear and A. E. Comarr. —p. 154.

Rehabilitation on the Job.—Keatinge says that although rehabilitation centers and physical therapy departments of hospitals play their part in the rehabilitation of the severely injured worker, the activities of these agencies lack the discipline of productive work, which is so important a factor in the rehabilitation of the workman. Conscious of the important part played by suitable work in rehabilitation, certain employers have set up special workshops for this purpose. In these workshops men carry out production jobs under special conditions, and although good results have been obtained, there are shortcomings. Even under good conditions the psychologic effect created by a number of injured persons working in one shop is not always good, and feelings of inferiority may develop. The employee who goes back to work with his mates is usually anxious to emulate their achievements; he is among friends and is not a "new body," as is the case in the special shop. Furthermore, the special shop is impractical in any but the organization employing great numbers of workers. Reviewing 47 cases from a factory employing 700 workers, the author says that *2* men who sustained fractures of the lower limb returned to work having lost less than seven weeks time. The leg of a patient who sustained a fracture of the patella was allowed to remain in the plaster for just over four weeks; in the man who had a Pott's fracture the length of time during which the leg was kept in a plaster case was a little more than five weeks. The men got about in their plaster cases as best they could, and as soon as they were free to do so they began to use their limbs naturally. The man who fractured his patella went back to his usual occupation as a crane driver, from which it may be inferred that there was little impairment of flexion at the knee joint. In the case of the man who had a Pott's fracture and whose work was that of a heavy laborer, arrangements were made to make a start on rough painting. In this work he was obliged to move about to some extent. Within eight weeks of his return to work he was back at his preaccident occupation, completely free from all pain or swelling and with full movement in his ankle joint. All of 44 men who had minor injuries went back to their jobs. Early return to work should always be in the surgeon's mind, and in the case of firms lacking a medical service the surgeon should himself approach the management with a view to placing their injured employees in suitable work as soon as their condition permits. The surgeon will find that industry will be ready to cooperate with him.

Ohio State Medical Journal, Columbus

45:317-428 (April) 1949

Surgical Risk in Patients with Heart Disease. P. M. Spurney.—p. 341.
Diagnosis of Herniation of Lumbar Intervertebral Disk (Nucleus Pulposus). R. E. Slemmer.—p. 345.
Objective Findings in Psychosomatic Dysfunction. C. deCourcy and J. E. Vollmer.—p. 349.
Mesenteric Commune: Report of Case. J. L. Bilton.—p. 351.
Ovarian Pregnancy: Case Report. J. P. Bolton.—p. 353.
Conservative Irradiation of Nasopharynx. H. H. Haggart.—p. 357.
Essential Dysmenorrhea—Its Pathogenesis and Treatment. L. B. Greentree.—p. 358.
Postoperative Care After Ileostomy. J. M. Walker.—p. 360.
Cystic Disease of Liver and Kidney: Report of Case. R. W. Urich. —p. 363.

Pennsylvania Medical Journal, Harrisburg

52:569-664 (March) 1949

Man Defends Himself. C. C. Dennie.—p. 585.
Vertigo: Diagnostic and Therapeutic Considerations. J. C. Yaskin.—p. 591.
Pennsylvania's School Health Program. S. J. Dickey.—p. 598.
Management of Industrial Ocular Injuries. H. M. Griffith.—p. 601.
Uterine Prolapse in Second Trimester of Pregnancy: Successful Treatment of Case. T. F. Hawkins.—p. 604.

52:665-792 (April) 1949

Physiologic Mechanisms of Psychosomatic Phenomena. S. Wolf, T. H. Holmes, H. Goodell and H. G. Wolff.—p. 681.
Nature of Emotional States That Disturb Bodily Function. O. S. English.—p. 689.
Psychosomatic Concept in General Medical Practice. E. Weiss.—p. 692.
Clinical Management of Deafness. K. M. Day.—p. 698.
Use of Propyl Thiouracil and of Radioactive Iodine. R. C. Grauer.—p. 704.
Management and Treatment of Pulmonary Tuberculosis with Streptomycin. G. E. Martin.—p. 708.
Treatment of Arthritis. R. Pemberton.—p. 712.
Significance of Symptoms and Roentgen Studies in Urinary Tract Disease. D. A. Sampson.—p. 715.
Topical Treatment of Lung Abscess. W. E. Burnett, G. P. Rosemond, H. T. Caswell and others.—p. 719.
Prostatism. E. F. Cosgrove.—p. 726.
Subdural Hematoma in Infants. J. F. Grunnagle.—p. 729.

Rhode Island Medical Journal, Providence

32:121-180 (March) 1949

X-Ray Treatment of Malignant Lymphoma. E. W. Benjamin.—p. 135.
Pathology of Malignant Lymphoma. R. J. Williams.—p. 137.
Simple Plastic Operation for Stenosed Colostomies. E. S. Cameron.—p. 138.
Diabetic Lipoidic Necrobiotic Dermatitis (Necrobiosis Lipoidica Diabeticorum Urbach). F. Ronchese and B. L. Schiff.—p. 139.
AMA's Plan of Battle: Outline of Strategy and Policies in Campaign Against Compulsory Health Insurance. C. Whitaker and L. Baxter.—p. 142.

32:181-240 (April) 1949

Radiologic Safety in Atomic Warfare. C. F. Behrens.—p. 195.
Sympathectomy—Its Role in Treatment of Vascular Disease. J. P. Eddy III.—p. 199.

Surgery, Gynecology and Obstetrics, Chicago

88:545-688 (May) 1949

Anatomic and Clinical Re-Evaluation of Camper's, Scarpa's, and Colles' Fasciae. C. E. Tobin and J. A. Benjamin.—p. 545.
*Gastric Resection for Esophagitis and Stricture of Acid-Peptic Origin. O. H. Wangensteen and N. L. Leven.—p. 560.
Surgical Treatment of Patent Ductus Arteriosus. W. J. Potts.—p. 571.
Anatomic Variations of Extrahepatic Biliary System as Seen by Cholangiographic Studies. N. F. Hicken, Q. B. Coray and B. Franz.—p. 577.
Rationale for Surgical Treatment of Duodenal Ulcer. R. A. Griswold.—p. 585.
*Mechanism of Intervertebral Disk Protrusion. F. H. Lewey.—p. 592.
Repair of Inguinal Hernia with External Oblique Fascia: Critical Evaluation of Results. C. W. Mayo and J. K. Keeley.—p. 603.
Surgical Treatment of Radiation Burns. J. B. Brown, F. McDowell and M. P. Fryer.—p. 669.
Imperforate Anus: Case Series and Preliminary Report on One Stage Abdominoperineal Operation. W. J. Norris, T. W. Brophy III and D. Brayton.—p. 623.
Trypsin and Thrombin Induced Venous Thrombosis and Its Prevention with Dicumarol, 3,3' Methylenebis (4 Hydroxycoumarin). W. D. Holden, D. B. Cameron, P. J. Shea Jr. and B. W. Shaw.—p. 635.
Evaluation of Hexachlorophene and Detergents as Substitutes for Surgical Scrub: Biological Technic. W. J. Nungester, R. L. Thirlby and A. B. Vial.—p. 639.
Tendon Transplants for Irreparable Radial Nerve Paralysis. C. Scuderi.—p. 643.
Ruptured Uterus: Report of 42 Cases. J. E. Fitzgerald, A. Webster and J. E. Fields.—p. 652.
Dextran: Experimental Plasma Substitute. F. P. Turner, B. C. Butler, M. E. Smith and J. Scudder.—p. 661.

Gastric Resection for Esophagitis of Acid-Peptic Origin.—Wangensteen and Leven say that a patient was operated on by Wangensteen in September 1939 for a massive hemorrhage from a duodenal ulcer. The patient had esophagitis, for which frequent esophageal dilatations had been done over a period of four years. An unexpected result of this operation was that dilatation of the esophageal stricture became unnecessary. Three years later, the same sequence of events was observed in another patient undergoing gastric resection for a gastrojejunal ulcer. This patient also had esophagitis necessitating esophageal dilatation. Therefore, when a third patient presented herself with a congenitally short esophagus, an esophageal stricture and gastric hemorrhage, it was reasoned that the stricture in this instance too might be occasioned by the regurgitation of hydrochloric acid into the lower reaches of the esophagus. A dramatic improvement followed gastric resection and helped confirm the impression that esophagitis and esophageal stricture might well be a consequence of the acid-peptic digestive mixture in the same manner that duodental ulcer is. Two additional patients with strictures fairly high in the esophagus were persuaded to accept the same operative procedure. A sixth case concerned a boy of 17 years with a stricture of the lower half of the esophagus. No ulcer could be demonstrated, but the gastric acids were high. Gastric resection was followed by complete relief of the difficulty in swallowing. These observations constitute evidence that esophagitis is a manifestation of ulcer disease.

Mechanism of Intervertebral Disk Protrusion.—Lewey says that the terms hidden or bulging disk and ruptured, herniating, protruded and slipped disk are sometimes used as if interchangeable. In reality, they denote different conditions. The author analyzes 40 cases of disk removal for sciatica. These cases represent part of a group of 169. Histologic examination of the 169 disks removed at operation and of 20 controls seems to suggest that the pathologic findings may be grouped into three classes, which differ widely in their mechanism and their surgical prognosis. They are: (1) The bulging disk without a rent in the annulus fibrosus and without detachment of the disk from the bone. Material removed by incision of the disk revealed normal cartilage lamellae. (2) The herniated disk in which traumatized disk lamellae are protruded through a rent of the annulus fibrosus into the spinal cavity where they may encroach on and overextend a posterior root. Herniation of the nucleus pulposus is the exception rather than the rule. (3) The slipped disk in which the trauma involves the cartilaginous epiphyseal plate and which is sometimes accompanied by a chip fracture of the vertebral rim. This frees the disk from its anchorage and permits an eccentric portion of its posterior circumference to slip backward. A posterior root may become hooked up over the protrusion. The sharp bony edges of the fracture may secondarily rupture the slipped disk. An individual constitutional disposition may be responsible for this type of lesion. This condition is visible in the roentgenogram. Trauma appears to be the only cause of herniation or slipping of the disk. The results of incision and dismemberment of a bulging disk are so poor as to suggest that in the 66 per cent of these patients not benefited by operation the bulging disk was not the cause of the sciatic syndrome. The inference is that the bulging disk should not be removed unless it clearly involves a root. The results of simple removal of the herniated disk are so satisfactory that there seems to be no need for further improvement of the operative technic. Operation on the slipped disk gives good to fair results in about one half of the persons operated on. The question is discussed under which conditions thorough removal of the disk may be indicated and when filling of the intervertebral space with bone chips or spinal fusion may be useful.

Wisconsin Medical Journal, Madison

48:207-296 (March) 1949

Leukemia Cutis of Scalp: Report of Case Involving Treatment by Roentgen Rays. E. A. Pohle and J. H. Juhl.—p. 223.
Pediatric Allergy. W. A. McGee.—p. 229.
Bronchiogenic Carcinoma. E. A. Graham.—p. 232.
Some Aspects of Treatment in Emotional Illness. H. M. Murdock.—p. 235.
Treatment of Leukemia. C. H. Watkins.—p. 239.
Surgical Treatment of Amebiasis. M. DeBakey and A. Ochsner.—p. 243.

48:297-388 (April) 1949

*Vitamin E Therapy in Heart Disease. G. L. Baum and W. Stein.—p. 315.
Use of Endocrine Substances in Obstetrics and Gynecology. P. F. Schneider.—p. 318.
Extreme Open-Bite Malocclusion Resulting from Improper Care of Complete Horizontal Fracture of Maxilla and Bilateral Fracture of Mandible. M. N. Federspiel.—p. 325.
Present Status of Vagotomy in Treatment of Peptic Ulcer. P. A. Midelfart.—p. 329.
Medical Care of Nation in Event of Another War. J. C. Sargent.—p. 335.
Eclamptic Toxemia. F. E. Whitacre and C. R. Green.—p. 339.

Vitamin E in Heart Disease.—Baum and Stein studied the effect of alphatocopherol on 22 unselected ambulatory patients with heart disease. The patients were given the drug in the recommended dosage. Only 2 received vitamin E alone; the remainder received other medication deemed necessary. The majority of the 22 patients showed no significant change in body weight, arm to tongue circulation time, vital capacity or blood pressure after oral administration of vitamin E in doses of 200 to 600 mg. daily for periods of nine to one hundred and fifty days. The majority of the 13 patients with the anginal syndrome either showed no improvement or became worse. The improvement noted in a small percentage could not be ascribed definitely to the action of alphatocopherol. No beneficial effect of vitamin E could be obtained in the majority of the 12 patients with hypertension. No improvement could be noted in 14 of 17 instances of cardiac failure. Six of these patients showed increasing congestive failure while receiving alphatocopherol. The reported benefits of administration of vitamin E in the treatment of patients with heart disease could not be substantiated.

FOREIGN

An asterisk (*) before a title indicates that the article is abstracted. Single case reports and trials of new drugs are usually omitted.

British Journal of Dermatology and Syphilis, London

61:113-156 (April) 1949

Clinical Reaction of Skin to Mustard Gas Vapor. D. C. Sinclair.—p. 113.
Epithelioma Arising on Lupus Erythematosus. G. E. W. Wolstenholme. —p. 126.
Case of Multiple Benign Angiomata. S. Canter.—p. 130.

61:157-196 (May) 1949

Kaposi's Varicelliform Dermatosis: Virus Pyodermia. T. Anderson. —p. 157.
Case of Kaposi's Varicelliform Eruption (Systemic Herpes Simplex) with Dendritic Ulceration of Cornea. R. Varley and T. Kletz. —p. 166.
Fatal Case of Kaposi's Varicelliform Eruption. J. C. Spry Leverton and F. A. Whitlock.—p. 170.

British Journal of Urology, London

21:1-100 (March) 1949

Etiologic and Therapeutic Experiences Concerning Kidney and Ureteric Stones. J. Hellström.—p. 9.
Bilateral Renal Calculi. J. T. Tait.—p. 17.
Radioscopy in Nephrolithotomy. N. J. Nicholson.—p. 24.
Tubular Calcification in Kidney. L. N. Pyrah.—p. 27.
Urinary Citrate Excretion in Patients with Renal Calculi. N. S. Conway, A. I. L. Maitland and J. B. Rennie.—p. 30.

British Medical Journal, London

1:737-790 (April 30) 1949

Basal-Cell Carcinoma (Rodent Ulcer), with Special Reference to Lesions on Neck, Trunk and Limbs. C. Wakeley and P. Childs.—p. 737.
*Streptomycin Treatment of Tuberculous Bronchopneumonia in Childhood. R. McL. Todd.—p. 741.
Some Practical Problems of Tuberculosis in Childhood. F. M. B. Allen. —p. 747.
*Effect of Endocrines on Fibro-Adenosis. H. J. B. Atkins.—p. 750.
*Curare-Modified Electric Convulsion Therapy in Cases with Physical Disease. P. D. W. Shepherd and D. C. Watt.—p. 752.

Streptomycin in Tuberculous Bronchopneumonia.—Todd reviews observations on 8 children from 5 months to 12 years of age, who were treated with streptomycin for tuberculous bronchopneumonia. This condition may simulate other types of bronchopneumonia, the main clinical differences being the insidious onset, steady progress of symptoms, increasing pallor, flabbiness and weakness, and the progressive character of the abnormal pulmonary signs in tuberculous bronchopneumonia. A history of contact and the isolation of Mycobacterium tuberculosis are important factors in the diagnosis. The streptomycin was given in the form of the hydrochloride. The dosage was 0.02 Gm. per pound of body weight every twenty-four hours, intramuscularly. The drug was dissolved in distilled water and was given in divided doses every six hours. This regimen was continued for twelve to twenty-two weeks. Three patients showed evidence of sensitivity to streptomycin. Two of the 8 patients have died, but even these survived for twelve weeks and nine and one-half months, respectively, after the start of streptomycin therapy. The 5 patients making good progress have survived sixteen, fifteen, ten, eight and four months after cessation of streptomycin therapy. Gain in weight and radiologic improvement in the lung fields are the two most valuable means of assessing progress. In 1 child tuberculous meningitis developed during treatment, and the organism became resistant to streptomycin. Of the 8 patients with proved tuberculous bronchopneumonia treated during the two years preceding the streptomycin trial, 7 died within four weeks after hospitalization.

Effect of Endocrine Substances on Fibroadenosis.—Atkins says that a clinic for investigation and treatment of the painful nodular breast was established at Guy's Hospital in 1937. The author attempted to investigate the effect of endocrine preparations on the disease called fibroadenosis, which is defined as "a painful or nodular condition of the breast not due to new growth, bacterial inflammation or fat necrosis." Thirty-three patients were given estrogen therapy. It was found that the estrogens are harmful if given in doses large enough to be effective, and that the larger the dose the more harmful is the effect. Histologically the fibroblastic reaction, the epitheliosis and the adenosis all tended to increase. Various androgen preparations were given by mouth, by injection, by inunction or by implantation. In a substantial proportion of cases androgen therapy caused temporary improvement in the symptoms of fibroadenosis, but the author believes that the effect is not sufficient to encourage its use in this condition.

Curare-Modified Electric Convulsion Therapy.—Shepherd and Watt report the results obtained in 50 patients whose physical condition rendered them unsuitable for ordinary electric convulsion therapy, but in whom this treatment, modified by curare, was used. This group included 20 patients with skeletal disease (many of whom had old fractures of the spine), 17 patients with cardiovascular disease, 4 with pulmonary tuberculosis and others who were extremely frail or senile. The authors used d-tubocurarine chloride to modify the convulsion. This was mixed with thiopental sodium and atropine, and the whole was given by rapid intravenous injection. Thiopental sodium was given to avoid apprehension and the unpleasant sensation of curarization and to facilitate artificial respiration. Atropine was employed to maintain a clear airway. In the patients susceptible to bone injury the advantages of diminishing the muscular contractions are obvious. Patients with hypertension are given curare because by diminishing the power of the muscular contractions the blood pressure is less affected than during an unmodified fit. It has also been shown in experiments that curare has a direct effect on the smooth muscle of blood vessels and tends therefore to reduce the blood pressure. In patients with congestive heart failure the strain on the circulation, and particularly the heart, is lessened. A suitable oxygen resuscitation apparatus must be available before this treatment is begun.

Edinburgh Medical Journal

56:1-40 (Jan.) 1949

Judgment in Cardiology. R. W. D. Turner.—p. 1.
Treatment of Carcinoma of Rectum with Special Reference to Preservation of Sphincter Mechanism. R. Mailer.—p. 13.

Journal of Laryngology and Otology, London

63:179-250 (April) 1949. **Partial Index**

Otologist and Rehabilitation of the Deaf. R. S. Stevenson.—p. 179.
Changes in Vestibular Reactions After Fenestration-Operation. L. B. W. Jongkees and J. Hulk.—p. 225.
Case of Osteomyelitis of Superior Maxilla Treated with Penicillin. T. M. Banham.—p. 233.
Case of Accessory Sinus Tuberculosis. W. G. R. Hore and W. Kirchenberger.—p. 235.

Lancet, London

1:719-762 (April 30) 1949

Chronic Bronchitis Never a Complete Diagnosis. W. A. Lister.—p. 719.
Observations on a Series of Labors with Special Reference to Physiologic Delivery. G. D. Read.—p. 721.
Curare-Like Action of Tri-(Diethylaminoethoxy)-Benzene Triethyliodide. W. W. Mushin, R. Wien, D. F. J. Mason and G. T. Langston. —p. 726.
*Streptomycin in Non-Tuberculous Infections. P. H. Buxton, Rosemary D. Simon and F. R. Selbie.—p. 729.
Experimental Observations on Renal Blood Flow. D. A. K. Black and M. G. Saunders.—p. 733.
Fatal Air Embolism During Blood Transfusion. G. B. Doyle and Patricia Frodsham.—p. 735.
*Hemochromatosis in Three Families and in a Woman. R. D. Lawrence. —p. 736.

Streptomycin in Nontuberculous Infections.—In January 1947 the Middlesex Hospital was invited to form one of the centers for investigating the value of streptomycin in the treatment of nontuberculous infections. Buxton and associates present the results to August 1948, when 67 patients had been treated. These include 44 with urinary infection, chiefly by Pseudomonas aeruginosa and Escherichia coli; 14 with wound infection, mainly by Staphylococcus albus and 9 with miscellaneous infections. Streptomycin was given only to patients in whom the infecting organism had been proved in vitro to be sensitive to streptomycin but insensitive to penicillin and the sulfonamide drugs. It was found that relatively large doses of streptomycin limited to a four day course in urinary infections due to a susceptible organism are likely to cure about a third of the patients, provided there is no mechanical obstruction to drainage that is producing an inaccessible nidus of infection. Any organisms still present after seventy-two hours showed greatly reduced sensitivity to streptomycin. It was therefore

concluded that no advantage was gained by giving streptomycin in adequate dosage for longer than four days in urinary infections, except in the rare event of the residual organism remaining sensitive to the drug. In staphylococcic infections resistant to other forms of chemotherapy the use of streptomycin has been promising. If improvement does not occur within a week of starting streptomycin therapy, further treatment by surgical means to eliminate inaccessible foci of infection and to provide adequate drainage should be considered. Side reactions to streptomycin were encountered in less than a third of the cases, and in only 3 cases, in which there was severe vestibular disturbance, were they of serious significance.

Hemochromatosis.—According to Lawrence, hemochromatosis, also known as bronzed diabetes, is rare. The first of the three families reviewed here had been reported previously. Of 6 males, 2 brothers definitely had the disease and 2 others probably had it. The second family consisted of the parents and 7 sons, of whom 4 were killed in the war (1914-1918). In 2 of the remaining sons bronzed diabetes developed at the ages of 52 and 59, respectively. The third family consisted of the parents and 5 sons, including a pair of identical twins. The father died at the age of 74 with severe diabetes and an enlarged liver, but he had neither splenomegaly nor pigmentation suggesting hemochromatosis. The 3 brothers of the twins seemed normal. The history of the identical twins revealed that at the age of 28 both had what was diagnosed as acholuric familial jaundice and both underwent splenectomy. At 34 one twin had "jaundice," and next year he had hepatitis with enlarged liver. When he was 36, diabetes developed. Nine months later after an attack of vomiting and cessation of insulin therapy the man died in diabetic coma. At necropsy microscopic study of sections disclosed every feature of hemochromatosis. At the age of 36 the other twin, during an attack of tonsillitis, was observed to have an enlarged liver. Later hemochromatosis was diagnosed. He died six months later, and widespread deposits of hemosiderin were found in all his organs. These twins present evidence of a genetic factor in hemochromatosis. The author cites the case of a woman who showed signs of diabetes at the age of 66. She became extremely dark and died three years later. Adrenal insufficiency was suspected from her asthenia and low blood pressure but was disproved by blood chemical tests. At necropsy typical deposits of iron were seen in all the organs examined, substantiating the clinical diagnosis of hemochromatosis. This was the only woman with hemochromatosis whom the author observed, although he had seen 39 men with this disorder. Sheldon's summary of cases listed 16 instances in women to 295 in men.

Medical Journal of Australia, Sydney

1:433-476 (April 2) 1949

Familial Lumbo-Sacral Syringomyelia and Significance of Developmental Errors of the Spinal Cord and Column. M. Jackson.—p. 433.
Post-Mortem Blood Sugar. J. I. Tonge and J. S. Wannan.—p. 439.
Criminal Responsibility in Incipient Psychosis. F. M. G. Prendergast.—p. 447.
Treatment of Neurosyphilis. L. B. Cox.—p. 449.
Recent Advances in Apparatus Used for Electroconvulsant Therapy and Electronarcosis. L. Wilson.—p. 451.
Gold Therapy in Rheumatoid Arthritis. L. J. A. Parr.—p. 453.
Human Toxoplasmosis, with Report of Case. A. R. Edmonds.—p. 456.
Aortitis Caused by Congenital Syphilis. C. Engel.—p. 458.
Some Observations on Recent Advances in Thoracic Surgery. H. D. Sutherland.—p. 459.

Proceedings of Royal Society of Medicine, London

42:115-200 (March) 1949. **Partial Index**

Anesthesia for Thyroid Surgery. S. Rowbotham.—p. 115.
Dental Sepsis and Chronic Rheumatism. G. D. Kersley.—p. 151.
Fibrositis in Muscles of Mastication. J. W. E. Snawdon.—p. 153.
Review of Treatment of Tuberculous Meningitis with Streptomycin. H. Cairns and Margaret Taylor.—p. 155.
Gross Morbid Anatomy of Central Nervous System of Cases of Tuberculous Meningitis Treated with Streptomycin. P. M. Daniel.—p. 169.
Surgical Anatomy of Ischiorectal Space: President's Address. C. N. Morgan.—p. 189.

42:201-282 (April) 1949. **Partial Index**

Section of Experimental Medicine and Therapeutics: Place of Experimental Method in Medicine. G. W. Pickering.—p. 229.
Dental Caries in Norwegian Children During and After the Last World War: Preliminary Report. G. Toverud.—p. 249.

Archivos de Pediatria del Uruguay, Montevideo

20:73-118 (Feb.) 1949. **Partial Index**

*Penicillin Aerosols in Pediatrics. C. A. Bauza.—p. 86.

Penicillin Aerosols in Pediatrics.—According to Bauza inhalation of penicillin aerosol is the treatment of choice for bronchopulmonary infections when these are caused by bacteria sensitive to penicillin. He reports favorable results from administration of nebulized penicillin aerosols in 7 patients, infants or children, with acute lung abscess, bronchiectasis and bronchopneumonia. The inhalation was practiced twice daily in a dose of 50,000 units of penicillin. The penicillin solution used was at a concentration of 25,000 units for 1 cc. of the solution. The treatment was administered for five to nine days. In some cases nebulization of sulfamide aerosols was used alternating with penicillin.

Praxis, Bern

38:339-352 (April 21) 1949

*Treatment of Urogenital Tuberculosis with Streptomycin. J. Cibert.—p. 339.
Vitamin A in Keratosis Follicularis and Similar Dermatoses. F. Oldenberg.—p. 343.

Streptomycin in Urogenital Tuberculosis.—Cibert treated 117 patients with urogenital tuberculosis with streptomycin. The daily dose of the drug was 2 Gm. in the majority of cases and occasionally 1 or 1.5 Gm. The total dose of the drug varied from 15 Gm. to 150 Gm., with an average total dose of 40 Gm. Streptomycin had a pronounced effect on recent and superficial lesions of the urinary mucosa but was not effective in ulcerative caseous lesions of the renal parenchyma. Streptomycin does not change the indications for nephrectomy in tuberculosis. The drug may be effective in ulcerative processes in their initial stage, provided the patient is admitted to a sanatorium and the treatment is continued for a prolonged period. Nephrectomy may become unnecessary as the result of the treatment with the drug in the initial stage of the disease. Streptomycin makes it possible to extend surgical treatment to the urinary lesions of patients with pulmonary tuberculosis. Streptomycin proved to be of value in preoperative treatment and as an adjuvant to surgical treatment by improving early and late results. In cases in which surgical treatment is not feasible or is inadequate, streptomycin should be combined with other measures in order to secure relief and to prolong the life span of the patient.

Schweizerische medizinische Wochenschrift, Basel

79:397-420 (May 7) 1949. **Partial Index**

Lesion of Brachial Plexus: Paralysis of "Full Pack" in Military Personnel. M. Jéquier.—p. 397.
*Prevention of Fractures During Electroshock Therapy by Means of Mesantoin. P. Plattner.—p. 402.
Sensorium and Sensibility Under Influence of Curare. H. Moser.—p. 408.
Break-Down and Build-Up as Metabolic Problems. H. W. Bansi.—p. 409.
Ultrasonic Waves in Medicine. V. Buchtala.—p. 412.

Mesantoin® to Prevent Fractures During Electroshock Therapy.—Plattner says that in 500 patients, 200 men and 300 women, electroshock therapy was given without medication designed to prevent fractures. This group included only those who had had at least three complete shock treatments. Fractures had been sustained by 18.5 per cent of the men and 7 per cent of the women. These injuries required cessation of the shock treatments in 10 per cent of the men and in 2 per cent of the women. Fractures of the vertebrae are the most frequent. Fractures of the humerus, of the neck of the femur and of the scapula, and dislocations of the shoulder and foot joints, although much less frequent than vetrebral fractures, are generally more serious with regard to the continuation of the shock treatment. The authors used mesantoin,® (3-methyl-5, 5-ethylphenylhydantoin) to prevent fractures. Beginning with one tablet of 0.1 Gm. of mesantoin® twice daily, the dose is gradually increased upward within a week in women up to four to six tablets and in men to six to eight tablets. Doses of from four to eight tablets daily are given throughout the period of treatment, even on the days on which electroshock treatment is not given. No fractures occurred in 130 patients given this drug and subjected to electric shock therapy.

Book Notices

A Primer of Electrocardiography. By George E. Burch, M.D., F.A.C.P., Henderson Professor of Medicine, Tulane University School of Medicine, New Orleans, La., and Travis Winsor, M.D., F.A.C.P., Assistant Clinical Professor of Medicine, University of Southern California Medical School, Los Angeles, Calif. Second edition. Cloth. Price, $4.50. Pp. 245, with 266 illustrations. Lea & Febiger, 600 S. Washington Sq., Philadelphia 6, 1949.

This is the second edition of an excellent introduction to electrocardiography. It is basically a thorough discussion of the theory upon which the ultimate interpretation of the electrocardiogram is based. The normal and pathologic characteristics of all the usually recognized leads—arm leads, single and multiple precordial leads, unipolar leads and esophageal leads—are amply covered. There is not a large list of photographs of electrocardiograms to be interpreted by the student. Rather, the mechanism responsible for various patterns of the electrocardiogram is amply discussed. With this basic understanding, the clinical application in reading electrocardiograms is based on a solid foundation. The subject matter is clearly presented. This work is highly recommended for the student and the beginner.

Variations in State Public Health Programs as Portrayed by the Annual Combined Report and Plan for the Fiscal Year 1948. By Josephine Campbell, Rubye F. Mullins and Marion Kennedy, Methods Examiners. From the Records and Reports Section, Bureau of State Services, United States Public Health Service, Federal Security Agency. Paper. Pp. 53, with 4 illustrations. Washington, D. C., 1949.

For the physician or other health worker interested in getting an over-all picture of state public health programs, this mimeographed pamphlet is a handy reference manual. Based on the annual combined state reports for 1947 and plans for 1948, it indicates trends for a wide range of activities, including cancer services, mental hygiene, school health services, industrial hygiene, laboratory services and tuberculosis and venereal disease control. The significant fact that most of the states lean heavily on federal aid is emphasized by the decreased operation of maternal and child health services in 1947 and continued cutbacks for 1948. As is pointed out, this is related directly to discontinuance of the Emergency Maternal and Infant Care Program.

Lack of trained personnel in practically all fields is stressed. As might be expected, most states planned extensive additions to mental hygiene staffs. One of the greatest increases accomplished and planned occurred in the field of laboratory services, with rather even distribution among all reporting agencies. Four figures and 37 tables provide an easy means of assimilating the summaries and comparisons. This pamphlet should be in the hands of every physician engaged in public health work.

Office Management for Health Workers. By Frances King and Louis L. Feldman. Cloth. Price, $2.25. Pp. 164, with 12 illustrations. Commonwealth Fund, Division of Publications, 41 E. 57th St., New York 22; Oxford University Press, Amen House, Warwick Sq., London, E.C.4, 1949.

First of its kind in a rapidly growing specialty that is receiving increased attention on all sides, this 164 page volume offers important assistance to workers at practically all levels. The 12 chapters include consideration of the office and staff, card files, correspondence, record forms, reports, surveys, case histories and budgets. The approach is so basic that the volume will be especially valuable to those new to this type of activity. As Stebbins states in his foreword, it should make an invaluable contribution to the effectiveness of a health office. Excellent illustrations are provided to emphasize significant points, and lists of equipment sources and reference books add to the practical assistance provided.

A Treatise on Contemporary Religious Jurisprudence. By I. H. Rubenstein. Cloth. Price $2.50. Pp. 120. The Waldain Press, P.O. Box 97, Chicago 90, 1948.

The interest of physicians in this book will be confined in the main to the second chapter, in which the author discusses the legal aspects, criminal and civil, of faith healing, including Christian science. There are generous references to and quotations from court decisions involving liability for failure on the part of parents to provide medical care for their children because of asserted religious beliefs and the relationship of Christian Science and other so-called forms of faith healing to medical practice acts. Included in the discussion of the civil aspects of the subject are references to the liability of Christian Scientists for malpractice, the effect of belief in faith healing on testamentary capacity, on qualification for jury service and as a ground for divorce. Chapters 1 and 3, respectively, take up the legal aspects of fortune telling and of pacifism as it relates to those who object to military service because of real or pretended religious beliefs. The value of the book lies in its references to pertinent court decisions, not in its literary merit.

Thank God for My Heart Attack. By Charles Yale Harrison. Cloth. Price, $2.50. Pp. 144. Henry Holt & Company, Inc., 257 Fourth Ave., New York 10, 1949.

Physicians may find reason for disagreement with some of Harrison's rather sweeping pronouncements but will be grateful for the basic principle that the patient with a heart attack must let his physician run the show. Harrison's bravado while he was in the clutches of his coronary attack might give some patients wrong ideas.

Additional excellent advice includes reassurance regarding vague chest pains and sensible discussion of the fact that vitamin E is not the "wonder drug" some have termed it for heart ailments. In an extensive discussion of smoking as a factor, data of considerable interest are presented. Also splendid is Harrison's dispassionate yet gentle reminder that as age advances the pace of daily living must be slowed.

Near the end of the volume the author presents a series of questions and answers. There is no clear elucidation of congenital heart disorders as differentiated from inherited tendencies toward development of specific heart diseases. Unfortunately, Harrison dismissed with a wave of the hand the possibility that overweight may be a factor in the development of heart abnormalities. Also unfortunate, in the light of recent scientific reports, is doubt of the value of anticoagulant therapy.

An Index of Treatment. By various writers. Edited by Sir Robert Hutchinson, Bt., M.D., LL.D., Consulting Physician, London Hospital, London, and Reginald Hilton, M.A., M.D., F.R.C.P., Physician to St. Thomas's Hospital, London. Thirteenth edition. Cloth. Price, $17. Pp. 972, with 100 illustrations. Williams & Wilkins Co., Mt. Royal & Guilford Aves., Baltimore 2, 1948.

Eight years have elapsed between the appearance of the twelfth and the present thirteenth edition of this well known book. It was hoped to publish a new edition three years ago but wartime difficulties of various sorts hindered the project. As in preceding editions, the roster of authors—currently reduced from 78 to 74—includes many of the most distinguished British specialists in practically all fields, and their contributions are of the high order to be expected from such a group. That some of the measures advocated are not in complete accord with American practice is really from our point of view an advantage, for the reader of the book on this side of the Atlantic will be enriched by making acquaintance with procedures—some more radical, others more conservative—that are variants of those he employs. The book is almost unbelievably inclusive.

Das Ekg-ABC: Eine Systematik zur Auswertung von Elektrokardiogrammen. Von Max Waldhecker. Paper. Pp. 114, with 135 illustrations. Georg Thieme, Diemershaldenstrasse 47, Stuttgart-O, 1948.

After a brief general discussion of cardiac anatomy and physiology, the various abnormalities of the different components of the electrocardiogram are listed and their meaning is discussed. Drawings are presented instead of actual records. The following examples are quoted in order to illustrate the erroneous statements made by the author: Disturbances of impulse conduction like sinoauricular block, auriculoventricular block and bundle branch block are listed as disturbances of impulse formation. Nonphasic sinus arrhythmia is stated to indicate myocardial damage. An instance of sinoauricular block where one of four sinus impulses is not followed by an auricular response is called 4:1 sinoauricular block. Passive nodal rhythm is interpreted as evidence of complete sinoauricular block. The common type of intraventricular block is called right bundle branch block and the uncommon type left bundle branch block, and later it is stated, "according to recent investigations the intraventricular block of the uncommon type may also be right

bundle branch block and only the Wilson block may be left bundle branch block."

The booklet fails to reflect the progress of electrocardiography made during the past fifteen years. This includes the important work on chest leads in the German literature published by F. Groedel and by M. Holzmann before World War II. It is revealing that G. Thieme, one of the outstanding publishers of medical literature at the time when German medical writing was at its best, today accepts such a totally inadequate book for publication.

Die geburtshilflichen Operationen: Ihre Ausführung und Anwendung: Ein Lehrbuch für Studierende und Gebrauchsbuch für Ärzte. Von Prof. Dr. med. Heinrich Martius, Direktor der Universitäts-Frauenklinik Göttingen. Sixth edition. Boards. Price, 15.60 marks. Pp. 287, with 281 illustrations. Georg Thieme, Diemershaldenstrasse 47, Stuttgart-O, 1948.

The appearance of six editions within fourteen years is sufficient proof that this book is popular. The author takes up the structure and forms of the birth canal and the baby, the mechanism of normal and abnormal labor, forceps operations, breech extraction, version, embryotomy, treatment of lacerations, operations for enlarging the birth canal, such as espisiotomy, cervical incisions, metreurysis, symphysiotomy, abdominal cesarean section, delivery of twins, treatment of prolapse of the cord, and arms, conduct of cases of placenta praevia, manual removal of the placenta, treatment of abortion and uterine tamponade, and operations to interrupt pregnancy and produce sterilization. Most of the 281 illustrations appear in the author's two volume "Lehrbuch der Geburtshilfe," but they are excellent and highly instructive. The illustration of the breech hook should be omitted because it is dangerous. Likewise, the drawing of the Credé expression of the placenta should be deleted for the same reason. Twenty pages and 27 illustrations are devoted to destructive operations, which is a disproportionately large amount of space and illustrations. In spite of these minor criticisms, the book is decidedly worth while because it was written by one of the leading obstetricians in Germany who demonstrates his extensive experience throughout the book. It is highly recommended for those who can read German.

Management of Common Gastro-Intestinal Diseases. Edited by Thomas A. Johnson. The American Practitioner Series. Fabrikold. Price, $7. Pp. 280, with 16 illustrations. J. B. Lippincott Co., 227-231 S. 6th St., Philadelphia 5, 1948.

The editor has selected capable gastroenterologists to write the chapters assigned to them. Unfortunately, some of the chapters, particularly that regarding the therapy of peptic ulcer, include material not substantiated by long-continued clinical experience.

One questions the validity of making a diagnosis of pancreatic diseases by means of determination of serum lipase and serum amylase only. Too much emphasis is apparently placed on the blood levels of serum lipase and amylase in the diagnosis of diseases of the pancreas.

Disease of the extrahepatic biliary passages is one of the most common digestive complaints, but is noteworthy by absence of consideration in this book. This statement is made in spite of the fact that the editor states in his preface that no attempt was made to cover the entire gastrointestinal field.

As a whole, the book is well written, in simple, understandable language, and is to be highly recommended to both students and practitioners.

Die Tuberkulose des Kindes: Ein Lehrbuch aus der Kinderheilstätte Wangen im Allgäu. Von Dr. med. habil. Heinrich Brüger, Dr. med. habil. Reiner W. Müller und Dr. Maria Birkenfeld. Boards. Pp. 340, with 209 illustrations. Georg Thieme, Diemershaldenstrasse 47, Stuttgart-O, 1948.

This book of 340 pages is devoted entirely to tuberculosis among children. In the introduction, attention is called to the high incidence of tuberculosis in Europe. The author does not regard congenital tuberculosis as an important problem. Under the heading of diagnostic aids, considerable importance is placed on the tuberculin test and the demonstration of tubercle bacilli. The discussion of primary tuberculosis includes the primary complex, with considerable emphasis on involvement of the bronchial lymph nodes. It is pointed out that evidence of disease seen in the parenchyma from the roentgen shadow it casts may be due to parenchymal inflammations or to atelectasis. The danger of atelectasis resulting in contraction of the involved part or bronchiectasis is emphasized. A large number of roentgenograms illustrate various stages in the evolution of primary tuberculosis and its complications.

Acute, fatal forms of tuberculosis, dependent on the primary type of the disease for their development, such as meningitis and miliary tuberculosis, are fully discussed. Once primary tuberculosis is established, all the other possibilities are presented, including the reinfection chronic forms of the disease. Under chemotherapy, various preparations are mentioned, but the sulfones and streptomycin are not discussed. Tuberculin therapy is given some consideration. All of the usual forms of treatment, such as collapse therapy, are presented.

About 20 pages are devoted to tuberculosis of the cervical and abdominal regions, with particular reference to involvement of the lymph nodes. This section is well illustrated and contains important points in diagnosis and treatment. The section on tuberculosis of the bones and joints consists of 86 pages and is profusely illustrated. The last chapter is limited to tuberculosis of the skin. This volume contains 209 illustrations and has a good index.

Die Lungentuberkulose: Eine Einführung. Von Dr. habil. Wilhelm Roloff, Chefarzt der Heilstätte Donaustauf bei Regensburg der LVA. Niederbayern-Oberpfalz. Cloth. Price, 9.60 marks. Pp. 138, with 31 illustrations. Springer-Verlag OHG, Jebensstrasse 1, Berlin-Charlottenburg 2, 1948.

This volume of only 138 pages contains a great deal of valuable information. A tuberculosis mortality graph for Prussia from 1876 to 1940 shows a decrease in the mortality rate from more than 300 per 100,000 in 1876 to less than 150 per 100,000 in 1914. There was then a sharp rise in the mortality rate to more than 250 per 100,000 in 1919. By 1924 the rate was again down to the 1914 level, and it continued to decrease to within the 50's per 100,000. Thus, within ten years after World War I began the mortality rate had reached its prewar level, and it continued downward at the same rate as prior to the war until 1940. It was well known that there was a rise in the mortality rate during World War II. However, the death rate now is apparently decreasing in a manner similar to that after World War I. The author has also shown graphically how in 1936 the mortality rate in Germany reached its height in the age group of approximately 65 years. After the age of about 30 years, rates among men were definitely higher than among women. At the age of 65 years the rate was almost 120 per 100,000 for men and less than 90 for women. This sex difference in mortality rate had continued through 1947.

Pulmonary tuberculosis is presented in considerable detail with reference to diagnosis and treatment. Chemotherapy, including antibiotic therapy, collapse therapy and other usual procedures are discussed at some length. The book contains 31 illustrations, mostly roentgenograms, six tables, a reference list and a good index.

Fetal and Neonatal Death: A Survey of the Incidence, Etiology, and Anatomic Manifestations of the Conditions Producing Death of the Fetus in Utero and the Infant in the Early Days of Life. By Edith L. Potter, M.D., Ph.D., Associate Professor in the Department of Obstetrics and Gynecology, the University of Chicago, and Fred L. Adair, M.D. Second edition. Cloth. Price, $3.75. Pp. 173, with 38 illustrations. University of Chicago Press, 58th St. & Ellis Ave., Chicago 37, 1949.

This volume is a revision of a book written and published originally in 1939. Dr. Potter and Dr. Adair have entered a field neglected by most authors and not at all well covered in medical literature. They have in general attempted to determine the cause of death in a period immediately after birth and preceding birth. The revision is more adequate than the original edition and contains the result of continued investigation and studies in this field of pathology. Especially excellent is the section concerned with the Rh factor and the influence which this factor has on death of the fetus and the baby in the neonatal period.

The authors have collected information relative to the effect of maternal German measles on the fetus. The book is splendidly written and especially valuable to all students of pathology, pediatrics, obstetrics and public health. It can be highly recommended to all physicians as an excellent contribution to a field not too well known or understood.

Queries and Minor Notes

THE ANSWERS HERE PUBLISHED HAVE BEEN PREPARED BY COMPETENT AUTHORITIES. THEY DO NOT, HOWEVER, REPRESENT THE OPINIONS OF ANY OFFICIAL BODIES UNLESS SPECIFICALLY STATED IN THE REPLY. ANONYMOUS COMMUNICATIONS AND QUERIES ON POSTAL CARDS WILL NOT BE NOTICED. EVERY LETTER MUST CONTAIN THE WRITER'S NAME AND ADDRESS, BUT THESE WILL BE OMITTED ON REQUEST.

AIR-FILTERING SYSTEMS FOR HAY FEVER

To the Editor:—One of my patients has hay fever and has consulted me as to the advisability of installing a window air-conditioning unit in her bedroom. I should appreciate your opinion about the extent of relief the patient may expect and whether there is any particular unit you would recommend.

David Bornstein, M.D., Paterson, N. J.

ANSWER.—Several kinds of filtering systems are available. The ideal system is placed in the air intake which serves the entire house. The most commonly used apparatus is the filter and fan combination placed in a window of the patient's bedroom (Arnett Air Filter, Arnett Air Filter Co., Chicago; Airgaard Filter, American Air Filter Co., Chicago). Some also provide cooling (Carrier Room Ventilator, Carrier Corp., Syracuse, N. Y.). A special apparatus (Ratheon Precipitator, Ratheon Corp., Chicago) which makes use of the principle of attraction of air particles to plates having a high electrostatic charge in addition to the filtering mechanism increases the effectiveness of particle removal. Too much is expected from filters. In the case of pollen and mold spores most of the exposure occurs during the daylight hours. The number of pollen or mold spores to which the patient is exposed during the night in his bedroom without a filter is about 5 to 20 per cent of that to which he could be exposed during the twenty-four hour period under usual conditions. One cannot expect too much benefit from a measure directed to a fraction of the sufferer's allergen exposure. If the patient is willing to stay in the prepared room the greater part of the twenty-four hours, the results can be, of course, much better.

SENSITIVITY TO A THINNER PENETRATOR

To the Editor:—An artist now teaching textile painting is experiencing sensitivity to Prang's textile colors penetrator thinner made by American Crayon Co. of New York. Can you tell me what the probable offending agent is or suggest a substitute thinner of a less allergic nature?

M.D., Montana.

ANSWER.—This query fails to inform one as to the nature and locus of the sensitivity. It is assumed that this condition is manifested by dermatitis; otherwise this reply is less valid. Prang's thinner penetrator is believed to approximate or simulate the following mixture: 35 per cent turpentine; 60 per cent NJ150, an aromatic petroleum solvent; 5 per cent high flash VM & P naphtha. Prang's thinner penetrator, purchased in open market, proved on casual skin patch testing to be a highly active primary irritant. Within one-half hour of contact, pronounced skin inflammation with discomfort appeared. Primary irritation is believed to constitute the chief action, but the possibility of allergic sensitivity is not denied. All of the possible constituents mentioned are known primary skin irritants. The selection of a wholly harmless substitute is difficult, since the technical requirement of a combined thinner penetrator calls for substances at least akin to those mentioned. However, it might prove expedient to employ turpentine alone, as this substance is perhaps the least active of the irritants involved. Further, it might prove practical to utilize a higher boiling point petroleum fraction, such as Stoddard's solvent, but equally good technical results are not assured. Pine oil as a penetrator may prove somewhat less irritating. For thinner alone it may prove possible to rely on a combination of known lesser irritants, such as one or more higher alcohols such as amyl alcohol, one or more esters such as ethyl acetate, and/or one or more ketones such as methyl ethyl ketone and possibly an aromatic such as toluene, although toluene exposure when high and sustained may induce systemic damage. Some protection may be gained by the application to the skin of nongreasy skin barriers, such as may be provided by the Milburn Company, Detroit, among others. It becomes obvious that extensive skin contact with any thinner penetrator of the type under discussion, in school instruction or elsewhere, is to be avoided. If contact is inevitable and substantial, the use of this item is attended by some risk of dermatitis.

INFANTILE CEREBRAL PALSY

To the Editor:—A male child, 17 months of age, has the following history: The mother's labor started at full term and was prolonged by five or six hours because of anterior colporrhaphy done ten months before onset of this pregnancy. The head was delivered with low forceps without any difficulty or traction. The baby seemed to develop normally but was rather listless. During the first month or two he had only one bowel movement per week. The baby was breast fed. At about 6 months he was unable to hold his head up well; it would fall forward toward his chest. A croupy cold developed several times with extreme croupy sound when the baby inhaled. These were treated with inhalations and phenobarbital atropine tablets. His muscles seemed atonic and flabby. When about 8 months old he was not able to sit up alone, but would fall forward. He has a ruddy complexion and fine but not abundant hair. When 1 year old he learned to clap hands and stood on his feet while holding onto something, but made no effort to crawl. At the age of 8 months, thyroid, whole gland substance, 2 to 4 grains per day, was begun, which he has received until now. He looks fine and is happy, yet he is much retarded for a baby of that age. Now at 17 months of age he does not make any effort to crawl, except backward. He pushes his walk toddle cart backward, but it has not taught him to walk. His knees seem wobbly. His teething has been irregular; he now has 10 teeth. The lower incisors are rather serrated, and the upper ones are chisel like. His features look normal. His anterior fontanel has closed to a great extent in the last three months, but it admits the tip of a finger. His bowel actions are now normal, even overactive at times, which I attribute to the thyroid administration. He has been fed S M A® (milk preparation) since 8 months of age and is rather fat, but not overly so. He has not talked yet, but tries to say "kitty" when he sees the cat. The other 4 children in the family are normal. This baby has had vitamin B tablets as well as radio-malt (a British malt extract preparation containing vitamins A, B_1, B_2 and D). The penis is small but normal in appearance. Both testicles are in the scrotum. He seldom cries. When the dessert is brought in he gets excited and refuses any more vegetables. He likes milk. When he hears singing, he sings too. Please suggest diagnosis, prognosis and treatment.

O. Rouhe, M.D., Kamina, Belgian Congo.

ANSWER.—Apparently this baby is suffering from infantile cerebral palsy. Probably he suffered meningeal or cerebral hemorrhage in the course of a somewhat prolonged labor, and to some degree to a vaginal wall obstruction, which is mentioned in the inquiry. Sometimes cerebral palsy is caused by a congenital malformation of cerebral structures, although this condition is relatively rare compared with hemorrhage at birth. The ultimate outcome in any single case is always doubtful. Some patients progress physically and mentally more than others, depending on the amount of cerebral damage sustained. Obviously, the amount of brain injury is difficult to determine.

From the clinical description surgical intervention does not seem indicated. No contractures or skeletal deformities are referred to in the case report. Braces would be without value, as they would only add extra weight to the already overburdened trunk and extremities. Prolonged bathing, permitting the child to splash and tumble, affords opportunity for muscular movements in the water, an excellent form of exercise. Avoid overfatigue, but encourage the child to exercise on the bed or floor by using his muscles freely. Allow the child to stand by the side of a table or chair, and assist him in making steps as if he were attempting to walk. Give him passive exercise by moving his back and extremities, supplemented with mild massage.

Nothing is to be gained by formal mental instruction at this time, except that which occurs in casual conversation and play with toys and picture books. Improvement at best is slow, though many of these patients make unexpected progress in time. The rearing of these children requires the greatest patience and forebearance on the part of parents and the family.

BCG VACCINATION

To the Editor:—My son, 22 years of age, has a negative reaction to tuberculin. He will soon be assigned to the Trudeau Foundation for the study of tuberculosis. Is it advisable to give him BCG inoculations preliminary to this assignment?

M.D., New York.

ANSWER.—Although BCG has been used for over twenty-five years, complete accord regarding its value in all situations is not noted. Levine (*Am. Rev. Tuberc.* **58**:581-582 [Nov.] 1948) contends that a rigid selection and control of the cases fails to show much advantage in vaccinated over unvaccinated persons. Myers (*Am. Rev. Tuberc.* **57**:107-109 [Jan.] 1948) believes that with good public health work BCG is not only unnecessary but is a detriment in producing tuberculin-positive reactions when tuberculin is used in case finding. In sparsely infected regions, there seems to be much merit in Myers' contentions. A large number of experienced investigators, however, have shown that tuberculin-negative persons vaccinated with BCG are less prone to have tuberculosis than unvaccinated

persons. The trend of opinion in this country now seems to be in favor of vaccination, especially where public health facilities are poor and in persons who are exposed to frequent and heavy infection, such as nurses, attendants, technicians, medical students and doctors in tuberculosis hospitals.

Since the person in question is going to a place of gross exposure to tubercle bacilli, vaccination with BCG is recommended.

CANKER SORES AND SMALLPOX VACCINATIONS

To the Editor:—I have been treating with smallpox vaccinations a 30 year old woman, who has multiple, severe, recurring canker sores of the mouth. There was a typical "take" to the first vaccination, and immune reaction followed each vaccination until ten had been given (at weekly intervals). Improvement occurred. Although a few canker sores formed, they were shallow and caused little pain. Gradually, however, the canker sores returned, and a second course was given. Again, the first vaccination resulted in a typical "take" and improvement followed. When the canker sores again became more severe a third series was started, and for the third time in a twelve month period a "take" resulted on the first vaccination of the series. I should like to ask the following questions: (1) Why should there be an apparent loss of immunity to the smallpox vaccination in such a short period of time? (2) Is there any way in which the immunity may be made more permanent? (3) Is there any other treatment you would recommend?

H. P. Van Cleve, M.D., Dodge Center, Minn.

ANSWER.—The case described has been given an excellent trial of vaccination therapy and can be used as an example of the etiologic aspects and treatment frequently associated with this condition. The newest knowledge of herpetic ulceration of the mouth indicates that it is caused by the virus that causes herpes simplex. Several conditions which have been mentioned as causes in the past probably act as conditioning factors to permit the virus to produce the lesions, e. g., vitamin B complex deficiency, hyperthyroidism, fevers, leukemias, menstruation, mild trauma and constitutional peculiarities. A typical feature of herpetic infection is that it does not produce an immunity of long standing. In the present instance the patient apparently did not have lasting immunity to the herpes virus as a result of cowpox vaccinations.

Studies by McNair Scott and associates in Philadelphia have shown that persons who have recurrent herpes exhibit a low antibody titer to the herpes simplex virus. Members of a family who have herpes have a low antibody titer. Patients with recurrent herpetic stomatitis often have difficulty in obtaining a "take" from smallpox vaccine (communication from Dr. Lester Burket, Philadelphia).

There would seem to be no way by which the immune period could be prolonged. One might try lengthening the time between vaccinations, but this at best is only as a matter of convenience. The patient should be studied thoroughly, and all adjunct methods used if they seem logical.

Allergy should be considered. Oral hygiene should be practiced. An emotional instability should be considered and, if present, treated. An antihistaminic drug could be tried. The newly developed antibiotics, particularly aureomycin, which have been effective against some viruses, might be kept in mind, although no reports of their use in conditions like the one described have been made.

ROCKY MOUNTAIN SPOTTED FEVER

To the Editor:—A man aged 30 discovered a flat tick loosely attached to his body on awakening. The tick could easily be removed. In such a case, should 2 cc. of Rocky Mountain spotted fever vaccine be given immediately and 2 cc. one week later, or should 1 cc. be given three times at weekly intervals, or should no medication be given? The patient was asymptomatic, and the tick was not attached longer than fourteen hours.

M.D., Colorado.

ANSWER.—Rocky Mountain spotted fever vaccine is probably of little value when administered after an infected tick bite. Probably ten days or more are required for immunity of this type to develop. If the patient in this case is likely to be exposed repeatedly, he may be immunized in the routine manner to protect him against possible infection from subsequent tick bites. There is relatively little difference between the two methods of administration indicated in the question, except that the use of 1 cc. for three injections is less likely to cause annoying reactions.

The efficacy of treatment of Rocky Mountain spotted fever has been so much improved by the discovery of the antibiotics chloramphenicol and aureomycin that the occurrence of a tick bite at rare intervals need no longer be regarded as seriously as once was the case, although it is still advisable to use all reasonable precautions against ticks in order to avoid bites.

APHTHOUS STOMATITIS

To the Editor:—A 21 year old married woman has a normal history, except for one attack of pyelitis, and aphthous stomatitis since early childhood. While she is never completely free, during menstruation her mouth shows numerous lesions. She has a temperature up to 102 F. and is unable to eat. She has been in hospitals several times and has received the following medication: penicillin, orally and intramuscularly; sulfathiazole; bismuth by injection; large doses of vitamin B complex; ascorbic acid, and numerous mouth washes, without any change in the clinical picture. At present she receives 1 tablet of cebefortis® (thiamine hydrochloride 5 mg., riboflavine 5 mg., pyridoxine 1.5 mg., calcium pentothenate 25 mg., nicotinamide 50 mg. and ascorbic acid 150 mg.) daily. She uses methylrosaniline chloride locally and 1 ampule of bismuth arsphenamine sulfonate (bismarsen®) weekly. That regimen seems to shorten the duration of the acute symptoms but has not cured her condition.

Ernest Burian, M.D., Sidney, N. Y.

ANSWER.—The cause of aphthous and herpetic stomatitis is the virus of herpes simplex, to which some persons may have little or no continued immunity. The susceptibility may be modified by secondary conditions. The lesions are recurrent, and they resist therapy with ordinary methods, such as have been used in this case. The most effective method of prevention is recurrent vaccination with smallpox vaccine. A series of eight or ten vaccinations are given, at intervals of a week or ten days, starting when the lesions are absent, if possible, and continuing regardless of "takes." The local use of estrogenic ointment has also been suggested. (See THE JOURNAL, July 10, 1948, page 1004.)

DRYNESS OF SKIN

To the Editor:—I have under my care a woman age 40, bipara, gravida II, who has been complaining of dryness of skin, lips and scalp for the past two years. Results of complete physical examination are negative. The blood, urine and radiographic observations are within normal limits. The only positive observations are retroversion and a small fibroid of the uterus. She was seen by a dermatologist, who expressed no opinion but advised the use of vitamin A (25,000 units) daily. There has been no change in her condition despite vitamin A therapy for over a year and the use of cold cream massages.

M.D., New York.

ANSWER.—It might be well in this case to increase the dosage of vitamin A to 100,000 units daily, and to apply to the skin an ointment that is softening and absorbed to some extent—one made with wool fat or aquaphor® (an oxycholesterol-petrolatum ointment base). Water for bathing should be softened by the addition of a starch product, and a soapless detergent should be used instead of soap. If the basal metabolic rate is low, therapy with thyroid substance is indicated, and perhaps estrogenic substances if there is reason to suspect early onset of menopause. It is assumed, of course, that possible irritants, such as from cosmetics or products used in housework, have been eliminated as causative factors in this case and that thorough studies have been made to rule out systemic factors, such as diabetes.

PROCAINE ADMINISTERED INTRAVENOUSLY

To the Editor:—There is a question in the Queries and Minor Notes of February 26 (page 616) relating to use of 1 per cent procaine hydrochloride intravenously in cardiac arrhythmias. The reply gives a misleading sense of security. It should be emphasized that 1 per cent procaine hydrochloride given intravenously is extremely dangerous because of effects on the central nervous system; it causes convulsions and respiratory arrest.

The cases cited in the reply are those of ventricular arrhythmias arising in patients anesthetized with cyclopropane. In these circumstances procaine hydrochloride is indicated because of the extreme gravity of the prognosis and because deep general anesthesia will prevent the convulsive state that this dose of the drug would otherwise precipitate. In addition, facilities for continuous oxygen administration and artificial respiration are available in operating rooms.

Further evidence exists to contradict the reply given, as procaine hydrochloride and its products of active hydrolysis have been shown to act primarily on ventricular premature contractions and ectopic ventricular rhythms. It usually is ineffective in tachycardias of supraventricular origin, as in paroxysmal auricular tachycardia or paroxysmal auricular fibrillation. Thus, even if a patient were subjected to profound anesthesia to prevent the central nervous system irritation, intravenous administration of procaine hydrochloride rarely would be the method of choice.

Dr. Brody and his co-workers at the Goldwater Memorial Hospital, New York, have done extensive pioneer work on the less toxic hydrolysis products of procaine—diethylaminoethanol—and clinical trials of this drug are being carried out at Montefiore Hospital, New York, which work confirms the observation that procaine and its hydrolysis products act primarily on ventricular rather than supraventricular arrhythmias. It should be emphasized that intravenous use of 1 per cent procaine hydrochloride is not a safe routine for use in cardiac arrhythmias in unanesthetized patients.

Naomi de Sola Pool, M.D., New York.